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Attorney Docket No. : ELITRA.001A

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For : GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN ESCHERICHIA COLI

Attorney : Daniel Hart

"Express Mail"

Mailing Label No. : EL531032262US

Date of Deposit : January 27, 2000

I hereby certify that the accompanying

Transmittal in Duplicate; Specification in 122 pages; 3 sheets of drawings; Sequence Listing in 240 pages; Sequence Submission Statement; Sequence Listing in computer readable format; Check(s) for Filing Fee(s); Return Prepaid Postcard

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ATTENTION: BOX PATENT APPLICATION

Sir:

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For: **GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN ESCHERICHIA COLI**

Enclosed are:

- (X) Three (3) sheet(s) of drawing.
- (X) Specification in 122 pages.
- (X) Sequence listing in 240 pages.
- (X) One (1) page Sequence Submission Statement.
- (X) Sequence Listing in computer readable format.
- (X) Return prepaid postcard.

CLAIMS AS FILED

FOR	NUMBER FILED	NUMBER EXTRA	RATE	FEE
Basic Fee			\$345	\$345
Total Claims	111 - 20 =	91 ×	\$9	\$819
Independent Claims	40 - 3 =	37 ×	\$39	\$1443
If application contains any multiple dependent claims(s), then add			\$130	\$130
TOTAL FILING FEE		\$2,737		

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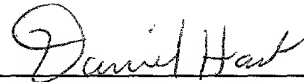
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Attorney Docket No. ELITRA.001A

Date: January 27, 2000

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**GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN
*ESCHERICHIA COLI***

RELATED APPLICATIONS

5 This application claims priority from U.S. Provisional Patent Application Serial Number 60/117,405 filed January 27, 1999, the disclosure of which is incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

10 Since the discovery of penicillin, the use of antibiotics to treat the ravages of bacterial infections has saved millions of lives. With the advent of these "miracle drugs," for a time it was popularly believed that humanity might, once and for all, be saved from the scourge of bacterial infections. In fact, during the 1980s and early 1990s, many large pharmaceutical companies cut back or eliminated antibiotics research and development. They believed that infectious disease caused by bacteria finally had been conquered and
15 that markets for new drugs were limited. Unfortunately, this belief was overly optimistic.

 The tide is beginning to turn in favor of the bacteria as reports of drug resistant bacteria become more frequent. The United States Centers for Disease Control announced that one of the most powerful known antibiotics, vancomycin, was unable to treat an infection of the common *Staphylococcus aureus* (staph). This organism is commonly
20 found in our environment and is responsible for many nosocomial infections. The import of this announcement becomes clear when one considers that vancomycin was used for years to treat infections caused by stubborn strains of bacteria, like staph. In short, the bacteria are becoming resistant to our most powerful antibiotics. If this trend continues, it is conceivable that we will return to a time when what are presently
25 considered minor bacterial infections are fatal diseases.

 There are a number of causes for the predicament in which practitioners of medical arts find themselves. Over-prescription and improper prescription habits by some physicians have caused an indiscriminate increase in the availability of antibiotics to the public. The patient is also partly responsible, for even in instances where an antibiotic is
30 the appropriate treatment, patients will often improperly use the drug, the result being yet another population of bacteria that is resistant, in whole or in part, to traditional antibiotics.

The bacterial scourges that have haunted humanity remain, in spite of the development of modern scientific practices to deal with the diseases that they cause. Drug resistant bacteria are now advancing on the health of humanity. A new generation of antibiotics to once again deal with the pending health threat that bacteria present is required.

Discovery of New Antibiotics

As more and more bacterial strains become resistant to the panel of available antibiotics, new compounds are required. In the past, practitioners of pharmacology would have to rely upon traditional methods of drug discovery to generate novel, safe and efficacious compounds for the treatment of disease. Traditional drug discovery methods involve blindly testing potential drug candidate-molecules, often selected at random, in the hope that one might prove to be an effective treatment for some disease. The process is painstaking and laborious, with no guarantee of success. Today, the average cost to discover and develop a new drug is nearly US \$500 million, and the average time is 15 years from laboratory to patient. Improving this process, even incrementally, would represent a huge advance in the generation of novel antimicrobial agents.

Newly emerging practices in drug discovery utilize a number of biochemical techniques to provide for directed approaches to creating new drugs, rather than discovering them at random. For example, gene sequences and proteins encoded thereby that are required for the proliferation of an organism make for excellent targets since exposure of bacteria to compounds active against these targets would result in the inactivation of the organism. Once a target is identified, biochemical analysis of that target can be used to discover or to design molecules that interact with and alter the functions of the target. Using physical and computational techniques, to analyze structural and biochemical targets in order to derive compounds that interact with a target is called rational drug design and offers great future potential. Thus, emerging drug discovery practices use molecular modeling techniques, combinatorial chemistry approaches, and other means to produce and screen and/or design large numbers of candidate compounds.

Nevertheless, while this approach to drug discovery is clearly the way of the future, problems remain. For example, the initial step of identifying molecular targets

for investigation can be an extremely time consuming task. It may also be difficult to design molecules that interact with the target by using computer modeling techniques. Furthermore, in cases where the function of the target is not known or is poorly understood, it may be difficult to design assays to detect molecules that interact with and alter the functions of the target. To improve the rate of novel drug discovery and development, methods of identifying important molecular targets in pathogenic microorganisms and methods for identifying molecules that interact with and alter the functions of such molecular targets are urgently required.

Escherichia coli represents an excellent model system to understand bacterial biochemistry and physiology. The estimated 4288 genes scattered along the 4.6×10^6 base pairs of the *Escherichia coli* (*E. coli*) chromosome offer tremendous promise for the understanding of bacterial biochemical processes. In turn, this knowledge will assist in the development of new tools for the diagnosis and treatment of bacteria-caused human disease. The entire *E. coli* genome has been sequenced, and this body of information holds a tremendous potential for application to the discovery and development of new antibiotic compounds. Yet, in spite of this accomplishment, the general functions or roles of many of these genes are still unknown. For example, the total number of proliferation-required genes contained within the *E. coli* genome is unknown, but has been variously estimated at around 200 to 700 (Armstrong, K.A. and Fan, D.P. Essential Genes in the *metB-malB* Region of *Escherichia coli* K12, 1975, J. Bacteriol. 126: 48-55).

Novel, safe and effective antimicrobial compounds are needed in view of the rapid rise of antibiotic resistant microorganisms. However, prior to this invention, the characterization of even a single bacterial gene was a painstaking process, requiring years of effort. Accordingly, there is an urgent need for more novel methods to identify and characterize bacterial genomic sequences that encode gene products required for proliferation and for methods to identify molecules that interact with and alter the functions of such genes and gene products.

SUMMARY OF THE INVENTION

One embodiment of the present invention is a purified or isolated nucleic acid sequence consisting essentially of one of SEQ ID NOs: 1-81, 405-485, wherein said

nucleic acid inhibits microorganism proliferation. The nucleic acid sequence may be complementary to at least a portion of a coding sequence of a gene whose expression is required for microorganism proliferation. The nucleic acid sequence may comprise a fragment of one of SEQ ID NOs. 1-81, 405-485, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 1-81, 405-485. The nucleic acid sequence may be complementary to a coding sequence of a gene whose expression is required for microorganism proliferation.

Another embodiment of the present invention is a vector comprising a promoter operably linked to a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 1-81, 405-485. The promoter may be active in an organism selected from the group consisting of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

Another embodiment of the present invention is a host cell containing the vectors described above.

Another embodiment of the present invention is a purified or isolated nucleic acid consisting essentially of the coding sequence of one of SEQ ID NOs: 82-88, 90-242. One aspect of this embodiment is a fragment of the nucleic acid comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

Another embodiment of the present invention is a vector comprising a promoter operably linked to the nucleic acids of the preceding embodiment.

Another aspect of the present invention is a purified or isolated nucleic acid comprising a nucleic acid sequence complementary to at least a portion of an intragenic

sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region within an operon encoding a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

5 Another embodiment of the present invention is a purified or isolated nucleic acid comprising a nucleic acid having at least 70% homology to a sequence selected from the group consisting of SEQ ID NOs 1-81, 405-485, 82-88, 90-242 or the sequences complementary thereto as determined using BLASTN version 2.0 with the default parameters. The nucleic acid may be from an organism selected from the group
10 consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae*
15 or any species falling within the genera of any of the above species.

Another embodiment of the present invention is a purified or isolated nucleic
20 acid consisting essentially of a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

25 Another embodiment of the present invention is a host cell containing the vector of the preceding embodiment.

Another embodiment of the present invention is purified or isolated polypeptide comprising the sequence of one of SEQ ID NOs: 243-357, 359-398.

30 Another embodiment of the present invention is purified or isolated polypeptide comprising a fragment of one of the polypeptides of SEQ ID NOs. 243-357, 359-398, said fragment selected from the group consisting of fragments comprising at least 5, at

least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the polypeptides of SEQ ID NOs.: 243-357, 359-398.

Another embodiment of the present invention is an antibody capable of specifically binding the polypeptide of the preceding embodiment.

5 Another embodiment of the present invention is method of producing a polypeptide, comprising introducing a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 into a cell. The method may further comprise the step of isolating said protein.

10 Another embodiment of the present invention is a method of inhibiting proliferation comprising inhibiting the activity or reducing the amount of a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 or inhibiting the activity or reducing the amount of a nucleic acid encoding said polypeptide.

15 Another embodiment of the present invention is method for identifying compounds which influence the activity of a polypeptide required for proliferation comprising:

contacting a polypeptide comprising a sequence selected from the group consisting of 243-357, 359-398 with a candidate compound; and

20 determining whether said compound influences the activity of said polypeptide.

The activity may be an enzymatic activity. The activity may be a carbon compound catabolism activity. The activity may be a biosynthetic activity. The activity may be a transporter activity. The activity may be a transcriptional activity. The activity may be a DNA replication activity. The activity may be a cell division activity.

25 Another embodiment of the present invention is a compound identified using the above method.

Another embodiment of the present invention is method for assaying compounds for the ability to reduce the activity or level of a polypeptide required for proliferation, comprising:

30 providing a target, wherein said target comprises the coding sequence of a sequence selected from the group consisting of SEQ ID NOs. 82-88, 90-242;

contacting said target with a candidate compound; and

measuring an activity of said target.

The target may be a messenger RNA molecule transcribed from a coding region of one of SEQ ID. NOs.: 82-88, 90-242 and said activity is translation of said messenger RNA. The target may be a coding region of one of SEQ ID. NOs. 82-88, 90-242 and said activity is transcription of said messenger RNA.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for identifying compounds which reduce the activity or level of a gene product required for cell proliferation comprising the steps of:

expressing an antisense nucleic acid against a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

contacting said sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

The cell may be selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells. The cell may be an *E. coli* cell. The cell may be from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. The antisense nucleic acid may be transcribed from an inducible promoter. The method may, further comprise the step of contacting said cell with a concentration of inducer which induces said antisense nucleic acid to a sublethal level. The sub-lethal concentration of said inducer may be such that growth inhibition is 8% or more. The inducer may be isopropyl-1-thio- β -D-galactoside. The growth inhibition

may be measured by monitoring optical density of a culture growth solution. The gene product may be a polypeptide. The gene product may be an RNA. The gene product may comprise a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

5 Another embodiment of the present invention is a compound identified using the method above.

10 Another embodiment of the present invention is a method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242 or with activity against the product of said gene into a population of cells expressing a gene. The compound may be an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-81, 405-485, or a proliferation-inhibiting portion thereof. The proliferation inhibiting portion of one of SEQ ID NOs. 1-81, 405-485 may be a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 1-81, 405-485. The compound may be a triple helix oligonucleotide.

15 Another embodiment of the present invention is a preparation comprising an effective concentration of an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-81, 405-485, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier. The proliferation-inhibiting portion of one of SEQ ID NOs. 1-81, 405-485 may comprise at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 1-81, 405-485.

20 Another embodiment of the present invention is a method for inhibiting the expression of a gene in an operon required for proliferation comprising contacting a cell in a cell population with an antisense nucleic acid, said cell expressing a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242, wherein said antisense nucleic acid comprises at least a proliferation-inhibiting portion of said operon in an antisense orientation that is effective in inhibiting expression of said gene. The antisense nucleic acid may be complementary to a sequence of a gene comprising one or more of SEQ ID NOs.: 82-88, 90-242. The antisense nucleic acid may be a sequence of one of SEQ ID NOs.: 1-81, 405-485, or a portion thereof. The cell may be contacted with said

antisense nucleic acid by introducing a plasmid which expresses said antisense nucleic acid into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a phage which expresses said antisense nucleic acid into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a sequence encoding said antisense nucleic acid into the chromosome of said cell into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a retron which expresses said antisense nucleic acid into said cell population. The cell may be contacted with said antisense nucleic acid by introducing a ribozyme into said cell-population, wherein a binding portion of said ribozyme is complementary to said antisense oligonucleotide. The cell may be contacted with said antisense nucleic acid by introducing a liposome comprising said antisense oligonucleotide into said cell. The cell may be contacted with said antisense nucleic acid by electroporation. The antisense nucleic acid may be a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242. The antisense nucleic acid may be an oligonucleotide.

Another embodiment of the present invention is a method for identifying bacterial strains comprising the steps of:

providing a sample containing a bacterial species; and
identifying a bacterial species using a species specific probe having a sequence selected from the group consisting of SEQ ID NOs. 1-81, 405-485, 82-88, 90-242.

Another embodiment of the present invention is a method for identifying a gene in a microorganism required for proliferation comprising:

- (a) identifying an inhibitory nucleic acid which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;
- (b) contacting a second microorganism with said inhibitory nucleic acid;
- (c) determining whether said inhibitory nucleic acid from said first microorganism inhibits proliferation of said second microorganism; and
- (d) identifying the gene in said second microorganism which is inhibited by said inhibitory nucleic acid.

Another embodiment of the present invention is a method for assaying a compound for the ability to inhibit proliferation of a microorganism comprising:

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- (a) identifying a gene or gene product required for proliferation in a first microorganism;
- (b) identifying a homolog of said gene or gene product in a second microorganism;
- (c) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said second microorganism;
- (d) contacting said second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
- (e) contacting the sensitized microorganism of step (d) with a compound; and
- (f) determining whether said compound inhibits proliferation of said sensitized microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized microorganism.

The step of identifying a gene involved in proliferation in a first microorganism may comprise:

introducing a nucleic acid comprising a random genomic fragment from said first microorganism operably linked to a promoter wherein said random genomic fragment is in the antisense orientation; and

comparing the proliferation of said first microorganism transcribing a first level of said random genomic fragment to the proliferation of said first microorganism transcribing a lower level of said random genomic fragment, wherein a difference in proliferation indicates that said random genomic fragment comprises a gene involved in proliferation.

The step of identifying a homolog of said gene in a second microorganism may comprise identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a database using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78 algorithm with the default parameters. The step of identifying a homolog of said gene in a second microorganism may comprise identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide by identifying nucleic acids which hybridize to said first gene. The step of identifying a homolog of said gene in a second microorganism may comprise expressing a nucleic acid which inhibits the proliferation of said first microorganism in said second microorganism. The inhibitory nucleic acid may be an antisense nucleic acid. The inhibitory nucleic acid may comprise an

antisense nucleic acid to a portion of said homolog. The inhibitory nucleic acid may comprise an antisense nucleic acid to a portion of the operon encoding said homolog. The step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence may comprise directly contacting said second
5 microorganism with said nucleic acid. The step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence may comprise expressing an antisense nucleic acid to said homolog in said second microorganism.

10 Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method of assaying a compound for the ability to inhibit proliferation comprising:

- 15 (a) identifying an inhibitory nucleic acid sequence which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;
(b) contacting a second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
(c) contacting the proliferation-inhibited microorganism of step (b) with a compound; and
20 (d) determining whether said compound inhibits proliferation of said sensitized second microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized second microorganism.

The inhibitory nucleic acid may be an antisense nucleic acid which inhibits the proliferation of said first microorganism. The inhibitory nucleic acid may comprise a portion of an antisense nucleic acid which inhibits the proliferation of said first
25 microorganism. The inhibitory nucleic acid may comprise an antisense molecule against the entire coding region of the gene involved in proliferation of the first microorganism. The inhibitory nucleic acid may comprise an antisense nucleic acid to a portion of the operon encoding the gene involved in proliferation of the first microorganism.

30 Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for assaying compounds for activity against a biological pathway required for proliferation comprising:

sensitizing a cell by expressing an antisense nucleic acid against a nucleic acid encoding a gene product required for proliferation in a cell to reduce the activity or amount of said gene product;

contacting the sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

The cell may be selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells. The cell may be an *E. coli* cell. The cell may be an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. The antisense nucleic acid may be transcribed from an inducible promoter. The method may further comprise contacting the cell with an agent which induces expression of said antisense nucleic acid from said inducible promoter, wherein said antisense nucleic acid is expressed at a sublethal level. The sublethal level of said antisense nucleic acid may inhibit proliferation by 8% or more. The agent may be isopropyl-1-thio- β -D-galactoside (IPTG). The inhibition of proliferation may be measured by monitoring the optical density of a liquid culture. The gene product may comprise a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for assaying a compound for the ability to inhibit cellular proliferation comprising:

contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell;

5 contacting said cell with said compound; and

determining whether said compound reduces proliferation to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.

10 The agent which reduces the activity or level of a gene product required for proliferation of said cell may comprise an antisense nucleic acid to a gene or operon required for proliferation. The agent which reduces the activity or level of a gene product required for proliferation of said cell may comprise an antibiotic. The cell may contain a temperature sensitive mutation which reduces the activity or level of said gene product required for proliferation of said cell. The antisense nucleic acid may be
15 directed against the same functional domain of said gene product required for proliferation of said cell to which said antisense nucleic acid is directed. The antisense nucleic acid may be directed against a different functional domain of said gene product required for proliferation of said cell than the functional domain to which said antisense nucleic acid is directed.

20 Another embodiment of the present invention is a compound identified using the method above.

Another embodiment of the present invention is a method for identifying the pathway in which a proliferation-required nucleic acid or its gene product lies comprising:

25 expressing a sublethal level of an antisense nucleic acid directed against said proliferation-required nucleic acid in a cell;

contacting said cell with an antibiotic, wherein the a biological pathway on which said antibiotic acts is known; and

30 determining whether said cell has a substantially greater sensitivity to said antibiotic than a cell which does not express said sublethal level of said antisense nucleic acid.

Another embodiment of the present invention is a method for determining the pathway on which a test compound acts comprising:

5 (a) expressing a sublethal level of an antisense nucleic acid directed against a proliferation-required nucleic acid in a cell, wherein the biological pathway in which said proliferation-required nucleic acid lies is known,

(b) contacting said cell with said test compound; and

(c) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said antisense nucleic acid.

10 The method may further comprise:

(d) expressing a sublethal level of a second antisense nucleic acid directed against a second proliferation-required nucleic acid in said cell, wherein said second proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

15 (e) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said second antisense nucleic acid.

Another embodiment of the present invention is a purified or isolated nucleic acid consisting essentially of one of SEQ ID NOs: 358, 399-402.

20 Another embodiment of the present invention is a purified or isolated nucleic acid comprising a sequence selected from the group consisting of 1-81, 405-485, 82-88, 90-242, 358, 399-402.

Another embodiment of the present invention is a compound which interacts with the gene or gene product of a nucleic acid comprising a sequence of one of SEQ ID NOs: 82-88, 90-242 to inhibit proliferation.

25 Another embodiment of the present invention compound which interacts with a polypeptide comprising one of SEQ ID NOs. 243-357, 359-398 to inhibit proliferation.

Another embodiment of the present invention is a compound which interacts with a nucleic acid comprising one of SEQ ID NOs: 358, 399-402 to inhibit proliferation.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is an IPTG dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing either an antisense clone to the *E. coli* ribosomal protein rplW (AS-rplW) which is required for protein synthesis and essential cell proliferation, or an antisense clone to the *elaD* (AS-*elaD*) gene which is not known to be involved in protein synthesis and which is also essential for proliferation.

Figure 2A is a tetracycline dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing antisense to rplW(AS-rplW) in the presence of 0, 20 or 50 μ M IPTG.

Figure 2B is a tetracycline dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing antisense to *elaD* (AS-*elaD*) in the presence of 0, 20 or 50 μ M IPTG.

Figure 3 is a graph showing the fold increase in tetracycline sensitivity of *E. coli* transfected with antisense clones to essential ribosomal proteins L23 (AS-rplW) and L7/L12 and L10 (AS-rplLrplJ). Antisense clones to genes known not to be involved in protein synthesis (*atpB/E*(AS-*atpB/E*), *visC* (AS-*visC*, *elaD* (AS-*elaD*), *yohH* (AS-*yohH*) are much less sensitive to tetracycline.

Definitions

By “biological pathway” is meant any discrete cell function or process that is carried out by a gene product or a subset of gene products. Biological pathways include enzymatic, biochemical and metabolic pathways as well as pathways involved in the production of cellular structures such cell walls. Biological pathways that are usually required for proliferation of microorganisms include, but are not limited to, cell division, DNA synthesis & replication, RNA synthesis (transcription), protein synthesis (translation), protein processing, protein transport, fatty acid biosynthesis, cell wall synthesis, cell membrane synthesis & maintenance, etc.

By “inhibit activity against a gene or gene product” is meant having the ability to interfere with the function of a gene or gene product in such a way as to decrease expression of the gene or to reduce the level or activity of a product of the gene. Agents which have activity against a gene include agents that inhibit transcription of the gene and agents that inhibit translation of the mRNA transcribed from the gene. In microorganisms, agents which have activity against a gene can act to decrease expression of the operon in which the gene resides or alter the processing of operon

RNA such as to reduce the level or activity of the gene product. The gene product can be a non-translated RNA such as ribosomal RNA, a translated RNA (mRNA) or the protein product resulting from translation of the gene mRNA. Of particular utility to the present invention are anti-sense RNAs that have activities against the operons or genes to which they specifically hybridize.

By "activity against a gene product" is meant having the ability to inhibit the function or to reduce the level or activity of the gene product in a cell.

By "activity against a protein" is meant having the ability to inhibit the function or to reduce the level or activity of the protein in a cell.

By "activity against nucleic acid" is meant having the ability to inhibit the function or to reduce the level or activity of the nucleic acid in a cell.

As used herein, "sublethal" means a concentration of an agent below the concentration required to inhibit all cell growth.

DETAILED DESCRIPTION OF THE INVENTION

The present invention describes a group of *E. coli* genes and gene families required for growth and/or proliferation. A proliferation-required gene or gene family is one where, in the absence of a gene transcript and/or gene product, growth or viability of the microorganism is reduced or eliminated. Thus, as used herein the terminology "proliferation-required" or "required for proliferation" encompasses sequences where the absence of a gene transcript and/or gene product completely eliminates cell growth as well as sequences where the absence of a gene transcript and/or gene product merely reduces cell growth. These proliferation-required genes can be used as potential targets for the generation of new antimicrobial agents. To achieve that goal, the present invention also encompasses novel assays for analyzing proliferation-required genes and for identifying compounds which interact with the gene products of the proliferation-required genes. In addition, the present invention contemplates the expression of genes and the purification of the proteins encoded by the nucleic acid sequences identified as required proliferation genes and reported herein. The purified proteins can be used to generate reagents and screen small molecule libraries or other candidate compound libraries for compounds that can be further developed to yield novel antimicrobial compounds. The present invention also describes methods for identification of homologous genes in organisms other than *E. coli*.

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The present invention utilizes a novel method to identify proliferation-required *E. coli* sequences. Generally, a library of nucleic acid sequences from a given source are subcloned or otherwise inserted into an inducible expression vector, thus forming an expression library. Although the insert nucleic acids may be derived from the chromosome of the organism into which the expression vector is to be introduced, because the insert is not in its natural chromosomal location, the insert nucleic acid is an exogenous nucleic acid for the purposes of the discussion herein. The term expression is defined as the production of an RNA molecule from a gene, gene fragment, genomic fragment, or operon. Expression can also be used to refer to the process of peptide or polypeptide synthesis. An expression vector is defined as a vehicle by which a ribonucleic acid (RNA) sequence is transcribed from a nucleic acid sequence carried within the expression vehicle. The expression vector can also contain features that permit translation of a protein product from the transcribed RNA message expressed from the exogenous nucleic acid sequence carried by the expression vector. Accordingly, an expression vector can produce an RNA molecule as its sole product or the expression vector can produce a RNA molecule that is ultimately translated into a protein product.

Once generated, the expression library containing the exogenous nucleic acid sequences is introduced into an *E. coli* population to search for genes that are required for bacterial proliferation. Because the library molecules are foreign to the population of *E. coli*, the expression vectors and the nucleic acid segments contained therein are considered exogenous nucleic acid.

Expression of the exogenous nucleic acid fragments in the test population of *E. coli* containing the expression vector library is then activated. Activation of the expression vectors consists of subjecting the cells containing the vectors to conditions that result in the expression of the exogenous nucleic acid sequences carried by the expression vector library. The test population of *E. coli* cells is then assayed to determine the effect of expressing the exogenous nucleic acid fragments on the test population of cells. Those expression vectors that, upon activation and expression, negatively impact the growth of the *E. coli* screen population were identified, isolated, and purified for further study.

A variety of assays are contemplated to identify nucleic acid sequences that negatively impact growth upon expression. In one embodiment, growth in *E. coli* cultures expressing exogenous nucleic acid sequences and growth in cultures not expressing these

sequences is compared. Growth measurements are assayed by examining the extent of growth by measuring optical densities. Alternatively, enzymatic assays can be used to measure bacterial growth rates to identify exogenous nucleic acid sequences of interest. Colony size, colony morphology, and cell morphology are additional factors used to evaluate growth of the host cells. Those cultures that failed to grow or grow with reduced efficiency under expression conditions are identified as containing an expression vector encoding a nucleic acid fragment that negatively affects a proliferation-required gene.

Once exogenous nucleic acid sequences of interest are identified, they are analyzed. The first step of the analysis is to acquire the nucleic acid sequence of the nucleic acid fragment of interest. To achieve this end, the insert in those expression vectors identified as containing a sequence of interest is sequenced, using standard techniques well known in the art. The next step of the process is to determine the source of the nucleic acid sequence.

Determination of sequence source is achieved by comparing the obtained sequence data with known sequences in various genetic databases. The sequences identified are used to probe these gene databases. The result of this procedure is a list of exogenous nucleic acid sequences corresponding to a list that includes novel bacterial genes required for proliferation as well as genes previously identified as required for proliferation.

The number of DNA and protein sequences available in database systems has been growing exponentially for years. For example, at the end of 1998, the complete sequences of *Caenorhabditis elegans*, *Saccharomyces cerevisiae* and nineteen bacterial genomes, including *E. coli* were available. This sequence information is stored in a number of databanks, such as GenBank (the National Center for Biotechnology Information (NCBI), and is publicly available for searching.

A variety of computer programs are available to assist in the analysis of the sequences stored within these databases. FastA, (W. R. Pearson (1990) "Rapid and Sensitive Sequence Comparison with FASTP and FASTA" Methods in Enzymology 183:63- 98), Sequence Retrieval System (SRS), (Etzold & Argos, SRS an indexing and retrieval tool for flat file data libraries. Comput. Appl. Biosci. 9:49-57, 1993) are two examples of computer programs that can be used to analyze sequences of interest. In one embodiment of the present invention, the BLAST family of computer programs,

which includes BLASTN version 2.0 with the default parameters, or BLASTX version 2.0 with the default parameters, is used to analyze nucleic acid sequences.

BLAST, an acronym for "Basic Local Alignment Search Tool," is a family of programs for database similarity searching. The BLAST family of programs includes: BLASTN, a nucleotide sequence database searching program, BLASTX, a protein database searching program where the input is a nucleic acid sequence; and BLASTP, a protein database searching program. BLAST programs embody a fast algorithm for sequence matching, rigorous statistical methods for judging the significance of matches, and various options for tailoring the program for special situations. Assistance in using the program can be obtained by e-mail at blast@ncbi.nlm.nih.gov.

Bacterial genes are often transcribed in polycistronic groups. These groups comprise operons, which are a collection of genes and intergenic sequences. The genes of an operon are co-transcribed and are often related functionally. Given the nature of the screening protocol, it is possible that the identified exogenous nucleic acid sequence corresponds to a gene or portion thereof with or without adjacent noncoding sequences, an intragenic sequence (i.e. a sequence within a gene), an intergenic sequence (i.e. a sequence between genes), a sequence spanning at least a portion of two or more genes, a 5' noncoding region or a 3' noncoding region located upstream or downstream from the actual sequence that is required for bacterial proliferation. Accordingly, determining which of the genes that are encoded within the operons are individually required for proliferation is often desirable.

In one embodiment of the present invention, an operon is dissected to determine which gene or genes are required for proliferation. For example, the RegulonDB DataBase described by Huerta et al. (*Nucl. Acids Res.* **26**:55-59, 1998), which may also be found on the website http://www.cifn.unam.mx/Computational_Biology/regulondb/, may be used to identify the boundaries of operons encoded within microbial genomes. A number of techniques that are well known in the art can be used to dissect the operon. In one aspect of this embodiment, gene disruption by homologous recombination is used to individually inactivate the genes of an operon that is thought to contain a gene required for proliferation.

Several gene disruption techniques have been described for the replacement of a functional gene with a mutated, non-functional (null) allele. These techniques generally

involve the use of homologous recombination. The method described by Link et al. (J. Bacteriol 1997 179:6228; incorporated herein by reference in it's entirety) serves as an excellent example of these methods as applicable to disruption of genes in *E. coli*. This technique uses crossover PCR to create a null allele with an in-frame deletion of the coding region of a target gene. The null allele is constructed in such a way that sequences adjacent to the wild type gene (ca. 500 bp) are retained. These homologous sequences surrounding the deletion null allele provide targets for homologous recombination so that the wild type gene on the *E. coli* chromosome can be replaced by the constructed null allele.

The crossover PCR amplification product is subcloned into the vector pKO3, the features of which include a chloramphenicol resistance gene, the counter-selectable marker *sacB*, and a temperature sensitive autonomous replication function. Following transformation of an *E. coli* cell population with such a vector, selection for cells that have undergone homologous recombination of the vector into the chromosome is achieved by growth on chloramphenicol at the non-permissive temperature of 43°C. Under these conditions, autonomous replication of the plasmid cannot occur and cell are resistant to chloramphenicol only if the chloramphenicol resistance gene has been integrated into the chromosome. Usually a single crossover event is responsible for this integration event such that the *E. coli* chromosome now contains a tandem duplication of the target gene consisting of one wild type allele and one deletion null allele separated by vector sequence.

This new *E. coli* strain containing the tandem duplication can be maintained at permissive temperatures in the presence of drug selection (chloramphenicol). Subsequently, cells of this new strain are cultured at the permissive temperature 30°C without drug selection. Under these conditions, the chromosome of some of the cells within the population will have undergone an internal homologous recombination event resulting in removal of the plasmid sequences. Subsequent culturing of the strain in growth medium lacking chloramphenicol but containing sucrose is used to select for such recombinative resolutions. In the presence of the counter-selectable marker *sacB*, sucrose is rendered into a toxic metabolite. Thus, cells that survive this counter-selection have lost both the plasmid sequences from the chromosome and the

autonomously replicating plasmid that results as a byproduct of recombinative resolution.

There are two possible outcomes of the above recombinative resolution via homologous recombination. Either the wild type copy of the targeted gene is retained on the chromosome or the mutated null allele is retained on the chromosome. In the case of an essential gene, a single copy of the null allele would be lethal and such cells should not be obtained by the above procedure when applied to essential genes. In the case of a non-essential gene, roughly equal numbers of cells containing null alleles and cells containing wild type alleles should be obtained. Thus, the method serves as a test for essentiality of the targeted gene: when applied to essential genes, only cells with a wild type allele on the chromosome will be obtained.

Other techniques have also been described for the creation of disruption mutations in *E. coli*. For example, Link et al. also describe inserting an in-frame sequence tag concomitantly with an in-frame deletion in order to simplify analysis of recombinants obtained. Further, Link et al. describe disruption of genes with a drug resistance marker such as a kanamycin resistance gene. Arigoni et al., (Arigoni, F. et al. A Genome-based Approach for the Identification of Essential Bacterial Genes, Nature Biotechnology 16: 851-856, the disclosure of which is incorporated herein by reference in its entirety) describe the use of gene disruption combined with engineering a second copy of a test gene such that the expression of the gene is regulated by and inducible promoter such as the arabinose promoter to test the essentiality of the gene. Many of these techniques result in the insertion of large fragments of DNA into the gene of interest, such as a drug selection marker. An advantage of the technique described by Link et al. is that it does not rely on an insertion into the gene to cause a functional defect, but rather results in the precise removal of the coding region. This insures the lack of polar effects on the expression of genes downstream from the target gene.

Recombinant DNA techniques can be used to express the entire coding sequences of the gene identified as required for proliferation, or portions thereof. The over-expressed proteins can be used as reagents for further study. The identified exogenous sequences are isolated, purified, and cloned into a suitable expression vector using methods well known in the art. If desired, the nucleic acids can contain the sequences encoding a signal peptide to facilitate secretion of the expressed protein.

Expression of fragments of the bacterial genes identified as required for proliferation is also contemplated by the present invention. The fragments of the identified genes can encode a polypeptide comprising at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 75, or more than 75 consecutive amino acids of a gene complementary to one of the identified sequences of the present invention. The nucleic acids inserted into the expression vectors can also contain sequences upstream and downstream of the coding sequence.

When expressing the coding sequence of an entire gene identified as required for bacterial proliferation or a fragment thereof, the nucleic acid sequence to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector can be any of the bacterial, insect, yeast, or mammalian expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon usage and codon bias of the sequence can be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, et al., U.S. Patent No. 5,082,767, incorporated herein by this reference. Fusion protein expression systems are also contemplated by the present invention.

Following expression of the protein encoded by the identified exogenous nucleic acid sequence, the protein is purified. Protein purification techniques are well known in the art. Proteins encoded and expressed from identified exogenous nucleic acid sequences can be partially purified using precipitation techniques, such as precipitation with polyethylene glycol. Chromatographic methods usable with the present invention can include ion-exchange chromatography, gel filtration, use of hydroxyapatite columns, immobilized reactive dyes, chromatofocusing, and use of high-performance liquid chromatography. Electrophoretic methods such one-dimensional gel electrophoresis, high-resolution two-dimensional polyacrylamide electrophoresis, isoelectric focusing, and others are contemplated as purification methods. Also, affinity chromatographic methods, comprising antibody columns, ligand presenting columns and other affinity

chromatographic matrices are contemplated as purification methods in the present invention.

5 The purified proteins produced from the gene coding sequences identified as required for proliferation can be used in a variety of protocols to generate useful antimicrobial reagents. In one embodiment of the present invention, antibodies are generated against the proteins expressed from the identified exogenous nucleic acid sequences. Both monoclonal and polyclonal antibodies can be generated against the expressed proteins. Methods for generating monoclonal and polyclonal antibodies are well known in the art. Also, antibody fragment preparations prepared from the produced antibodies discussed above are contemplated.

10 Another application for the purified proteins of the present invention is to screen small molecule libraries for candidate compounds active against the various target proteins of the present invention. Advances in the field of combinatorial chemistry provide methods, well known in the art, to produce large numbers of candidate compounds that can have a binding, or otherwise inhibitory effect on a target protein. Accordingly, the screening of small molecule libraries for compounds with binding affinity or inhibitory activity for a target protein produced from an identified gene sequence is contemplated by the present invention.

15 The present invention further contemplates utility against a variety of other pathogenic organisms in addition to *E. coli*. For example, the invention has utility in identifying genes required for proliferation in prokaryotes and eukaryotes. For example, the invention has utility with protists, such as *Plasmodium* spp.; plants; animals, such as *Entamoeba* spp. and *Contracaecum* spp; and fungi including *Candida* spp., (e.g., *Candida albicans*), *Saccharomyces cerevisiae*, *Cryptococcus neoformans*, and *Aspergillus fumigatus*. In one embodiment of the present invention, monera, specifically bacteria are probed in search of novel gene sequences required for proliferation. This embodiment is particularly important given the rise of drug resistant bacteria.

20 The numbers of bacterial species that are becoming resistant to existing antibiotics are growing. A partial list of these organisms includes: *Staphylococcus* spp., such as *S. aureus*; *Enterococcus* spp., such as *E. faecalis*; *Pseudomonas* spp., such as *P. aeruginosa*, *Clostridium* spp., such as *C. botulinum*, *Haemophilus* spp., such as *H. influenzae*, *Enterobacter* spp., such as *E. cloacae*, *Vibrio* spp., such as *V. cholera*;

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Moraxala spp., such as *M. catarrhalis*; *Streptococcus* spp., such as *S. pneumoniae*,
Neisseria spp., such as *N. gonorrhoeae*; *Mycoplasma* spp., such as *Mycoplasma*
pneumoniae; *Salmonella typhimurium*; *Helicobacter pylori*; *Escherichia coli*; and
Mycobacterium tuberculosis. The sequences identified as required for proliferation in
5 the present invention can be used to probe these and other organisms to identify
homologous required proliferation genes contained therein.

In one embodiment of the present invention, the nucleic acid sequences disclosed
herein are used to screen genomic libraries generated from bacterial species of interest
other than *E. coli*. For example, the genomic library may be from *Staphylococcus aureus*,
10 *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria*
gonorrhoeae, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus*
influenzae, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*,
Cryptococcus neoformans, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella*
typhi, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*,
15 *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus*
anthracis, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, *Chlamydia*
trachomatis, *Chlamydia pneumoniae* or any species falling within the genera of any of
the above species. Standard molecular biology techniques are used to generate genomic
libraries from various microorganisms. In one aspect, the libraries are generated and
20 bound to nitrocellulose paper. The identified exogenous nucleic acid sequences of the
present invention can then be used as probes to screen the libraries for homologous
sequences. The homologous sequences identified can then be used as targets for the
identification of new, antimicrobial compounds with activity against more than one
organism.

25 For example, the preceding methods may be used to isolate nucleic acids having
a sequence with at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at
least 70% identity to a nucleic acid sequence selected from the group consisting of one
of the sequences of SEQ ID NOS. 1-81, 405-485, 82-88, 90-242, fragments comprising
at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive
30 bases thereof, and the sequences complementary thereto. Identity may be measured
using BLASTN version 2.0 with the default parameters. (Altschul, S.F. et al. Gapped
BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs,

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Nucleic Acid Res. 25: 3389-3402 (1997), the disclosure of which is incorporated herein by reference in its entirety). For example, the homologous polynucleotides may have a coding sequence which is a naturally occurring allelic variant of one of the coding sequences described herein. Such allelic variants may have a substitution, deletion or addition of one or more nucleotides when compared to the nucleic acids of SEQ ID NOs: 1-81, 405-485, 82-88, 90-242 or the sequences complementary thereto.

Additionally, the above procedures may be used to isolate nucleic acids which encode polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, or at least 40% identity or similarity to a polypeptide having the sequence of one of SEQ ID NOs: 243-357, 359-398 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof as determined using the FASTA version 3.0t78 algorithm with the default parameters. Alternatively, protein identity or similarity may be identified using BLASTP with the default parameters, BLASTX with the default parameters, or TBLASTN with the default parameters. (Alschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res. 25: 3389-3402 (1997), the disclosure of which is incorporated herein by reference in its entirety).

Alternatively, homologous nucleic acids or polypeptides may be identified by searching a database to identify sequences having a desired level of homology to a nucleic acid or polypeptide involved in proliferation or an antisense nucleic acid to a nucleic acid involved in microbial proliferation. A variety of such databases are available to those skilled in the art, including GenBank and GenSeq. In some embodiments, the databases are screened to identify nucleic acids or polypeptides having at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, or at least 50%, at least 40% identity or similarity to a nucleic acid or polypeptide involved in proliferation or an antisense nucleic acid involved in proliferation. For example, the database may be screened to identify nucleic acids homologous to one of SEQ ID Nos. 1-81, 405-485, 82-88, 90-242 or polypeptides homologous to SEQ ID NOs. 243-357, 359-398. In some embodiments, the database may be screened to identify homologous nucleic acids or polypeptides from organisms other than *E. coli*, including organisms such as *Staphylococcus aureus*, *Pseudomonas*

Gene expression arrays may be used to analyze the total mRNA expression pattern at various time points after induction of an antisense nucleic acid against a proliferation-required gene. Analysis of the expression pattern indicated by hybridization to the array provides information on whether or not the target gene of the antisense nucleic acid is being affected by antisense induction, how quickly the antisense is affecting the target gene, and for later timepoints, what other genes are affected by antisense expression. For example, if the antisense is directed against a gene for ribosomal protein L7/L12 in the 50S subunit, its targeted mRNA may disappear first and then other mRNAs may be observed to increase, decrease or stay the same. Similarly, if the antisense is directed against a different 50S subunit ribosomal protein mRNA (e.g. L25), that mRNA may disappear first followed by changes in mRNA expression that are similar to those seen with the L7/L12 antisense expression. Thus, the mRNA expression pattern observed with an antisense nucleic acid against a proliferation required gene may identify other proliferation-required nucleic acids in the same pathway as the target of the antisense nucleic acid. In addition, the mRNA expression patterns observed with candidate drug compounds may be compared to those observed with antisense nucleic acids against a proliferation-required nucleic acid. If the mRNA expression pattern observed with the candidate drug compound is similar to that observed with the antisense nucleic acid, the drug compound may be a promising therapeutic candidate. Thus, the assay would be useful in assisting in the selection of candidate drug compounds for use in screening methods such as those described below.

In cases where the source of nucleic acid deposited on the array and the source of the nucleic acid being hybridized to the array are from two different organisms, gene expression arrays can identify homologous genes in the two organisms.

The present invention also contemplates additional methods for screening other microorganisms for proliferation-required genes. In this embodiment, the conserved portions of sequences identified as proliferation-required can be used to generate degenerate primers for use in the polymerase chain reaction (PCR). The PCR technique is well known in the art. The successful production of a PCR product using degenerate probes generated from the sequences identified herein would indicate the presence of a homologous gene sequence in the species being screened. This homologous gene is then isolated, expressed, and used as a target for candidate antibiotic compounds. In another

aspect of this embodiment, the homologous gene is expressed in an autologous organism or in a heterologous organism in such a way as to alter the level or activity of a homologous gene required for proliferation in the autologous or heterologous organism. In still another aspect of this embodiment, the homologous gene or portion is expressed in an antisense orientation in such a way as to alter the level or activity of a nucleic acid required for proliferation of an autologous or heterologous organism.

The homologous sequences to proliferation-required genes identified using the techniques described herein may be used to identify proliferation-required genes of organisms other than *E. coli*, to inhibit the proliferation of organisms other than *E. coli* by inhibiting the activity or reducing the amount of the identified homologous nucleic acid or polypeptide in the organism other than *E. coli*, or to identify compounds which inhibit the growth of organisms other than *E. coli* as described below.

In another embodiment of the present invention, *E. coli* sequences identified as required for proliferation are transferred to expression vectors capable of function within non-*E. coli* species. As would be appreciated by one of ordinary skill in the art, expression vectors must contain certain elements that are species specific. These elements can include promoter sequences, operator sequences, repressor genes, origins of replication, ribosomal binding sequences, termination sequences, and others. To use the identified exogenous sequences of the present invention, one of ordinary skill in the art would know to use standard molecular biology techniques to isolate vectors containing the sequences of interest from cultured bacterial cells, isolate and purify those sequences, and subclone those sequences into an expression vector adapted for use in the species of bacteria to be screened.

Expression vectors for a variety of other species are known in the art. For example, Cao et al. report the expression of steroid receptor fragments in *Staphylococcus aureus*. **J. Steroid Biochem Mol Biol.** 44(1):1-11 (1993). Also, Pla et al. have reported an expression vector that is functional in a number of relevant hosts including: *Salmonella typhimurium*, *Pseudomonas putida*, and *Pseudomonas aeruginosa*. **J. Bacteriol.** 172(8):4448-55 (1990). These examples demonstrate the existence of molecular biology techniques capable of constructing expression vectors for the species of bacteria of interest to the present invention.

Following the subcloning of the identified nucleic acid sequences into an expression vector functional in the microorganism of interest, the identified nucleic acid sequences are conditionally transcribed to assay for bacterial growth inhibition. Those expression vectors found to contain sequences that, when transcribed, inhibit bacterial growth are compared to the known genomic sequence of the pathogenic microorganism being screened or, if the homologous sequence from the organism being screened is not known, it may be identified and isolated by hybridization to the proliferation-required *E. coli* sequence of interest or by amplification using primers based on the proliferation-required *E. coli* sequence of interest as described above.

The antisense sequences from the second organism which are identified as described above may then be operably linked to a promoter, such as an inducible promoter, and introduced into the second organism. The techniques described herein for identifying *E. coli* genes required for proliferation may thus be employed to determine whether the identified sequences from a second organism inhibit the proliferation of the second organism.

Antisense nucleic acids required for the proliferation of organisms other than *E. coli* or the genes corresponding thereto, may also be hybridized to a microarray containing the *E. coli* ORFs to gauge the homology between the *E. coli* sequences and the proliferation-required nucleic acids from other organisms. For example, the proliferation-required nucleic acid may be from *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni* or *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species. The proliferation-required nucleic acids from an organism other than *E. coli* may be hybridized to the array under a variety of conditions which permit hybridization to occur when the probe has different levels of homology to the sequence on the

microarray. This would provide an indication of homology across the organisms as well as clues to other possible essential genes in these organisms.

In still another embodiment, the exogenous nucleic acid sequences of the present invention that are identified as required for bacterial growth or proliferation can be used as antisense therapeutics for killing bacteria. The antisense sequences can be directed against the proliferation-required genes whose sequence corresponds to the exogenous nucleic acid probes identified here (i.e. the antisense nucleic acid may hybridize to the gene or a portion thereof). Alternatively, antisense therapeutics can be directed against operons in which proliferation-required genes reside (i.e. the antisense nucleic acid may hybridize to any gene in the operon in which the proliferation-required genes reside). Further, antisense therapeutics can be directed against a proliferation-required gene or portion thereof with or without adjacent noncoding sequences, an intragenic sequence (i.e. a sequence within a gene), an intergenic sequence (i.e. a sequence between genes), a sequence spanning at least a portion of two or more genes, a 5' noncoding region or a 3' noncoding region located upstream or downstream from the actual sequence that is required for bacterial proliferation or an operon containing a proliferation-required gene.

In addition to therapeutic applications, the present invention encompasses the use of nucleic acid sequences complementary to sequences required for proliferation as diagnostic tools. For example, nucleic acid probes complementary to proliferation-required sequences that are specific for particular species of microorganisms can be used as probes to identify particular microorganism species in clinical specimens. This utility provides a rapid and dependable method by which to identify the causative agent or agents of a bacterial infection. This utility would provide clinicians the ability to prescribe species specific antimicrobial compounds to treat such infections. In an extension of this utility, antibodies generated against proteins translated from mRNA transcribed from proliferation-required sequences can also be used to screen for specific microorganisms that produce such proteins in a species-specific manner.

The following examples teach the genes of the present invention and a subset of uses for the *E. coli* genes identified as required for proliferation. These examples are illustrative only and are not intended to limit the scope of the present invention.

EXAMPLES

The following examples are directed to the identification and exploitation of *E. coli* genes required for proliferation. Methods of gene identification are discussed as well as a variety of methods to utilize the identified sequences.

5 **Genes Identified as Required for Proliferation of *E. coli***

Exogenous nucleic acid sequences were cloned into an inducible expression vector and assayed for growth inhibition activity. Example 1 describes the examination of a library of exogenous nucleic acid sequences cloned into IPTG-inducible expression vectors. Upon activation or induction, the expression vectors produced an RNA molecule
10 corresponding to the subcloned exogenous nucleic acid sequences. The RNA product was in an antisense orientation with respect to the *E. coli* genes from which it was originally derived. This antisense RNA then interacted with sense mRNA produced from various *E. coli* genes and interfered with or inhibited the translation of the sense messenger RNA (mRNA) thus preventing protein production from these sense mRNA molecules. In cases
15 where the sense mRNA encoded a protein required for the proliferation, bacterial cells containing an activated expression vector failed to grow or grew at a substantially reduced rate.

EXAMPLE 1

Inhibition of Bacterial Proliferation after IPTG induction

20 To study the effects of transcriptional induction in liquid medium, growth curves were carried out by back diluting cultures 1:200 into fresh media with or without 1 mM IPTG and measuring the OD₄₅₀ every 30 minutes (min). To study the effects of transcriptional induction on solid medium, 10², 10³, 10⁴, 10⁵, 10⁶, 10⁷ and 10⁸ fold dilutions of overnight cultures were prepared. Aliquots of from 0.5 to 3 µl of these
25 dilutions were spotted on selective agar plates with or without 1 mM IPTG. After overnight incubation, the plates were compared to assess the sensitivity of the clones to IPTG.

Of the numerous clones tested, some clones were identified as a containing sequence that inhibited *E. coli* growth after IPTG induction. Accordingly, the gene to
30 which the inserted nucleic acid sequence corresponds, or a gene within the operon containing the inserted nucleic acid, may be required for proliferation in *E. coli*.

Characterization of Isolated Clones Negatively Affecting *E. coli* Proliferation

Following the identification of those expression vectors that, upon expression, negatively impacted *E. coli* growth or proliferation, the inserts or nucleic acid fragments contained in those expression vectors were isolated for subsequent characterization.

5 Expression vectors of interest were subjected to nucleic acid sequence determination.

EXAMPLE 2

Nucleic Acid Sequence Determination of Identified Clones Expressing Nucleic Acid Fragments with Detrimental Effects of *E. coli* Proliferation

10 The nucleotide sequences for the exogenous identified sequences were determined using plasmid DNA isolated using QIAPREP (Qiagen, Valencia, CA) and methods supplied by the manufacturer. The primers used for sequencing the inserts were 5' - TGTTTATCAGACCGCTT - 3' (SEQ ID NO: 403) and 5' - ACAATTTACACAGCCTC - 3' (SEQ ID NO: 404). These sequences flank the polylinker in pLEX5BA. Sequence identification numbers (SEQ ID NOs) for the
15 identified inserts are listed in Table I and discussed below.

EXAMPLE 3

Comparison Of Isolated Sequences to Known Sequences

20 The nucleic acid sequences of the subcloned fragments obtained from the expression vectors discussed above were compared to known *E. coli* sequences in GenBank using BLAST version 1.4 or version 2.0.6 using the following default parameters: Filtering off, cost to open a gap=5, cost to extend a gap=2, penalty for a mismatch in the blast portion of run=-3, reward for a match in the blast portion of run=1, expectation value (e)=10.0, word size=11, number of one-line descriptions=100, number of alignments to show (B)=100. BLAST is described in Altschul, J Mol Biol. 215:403-10
25 (1990), the disclosure of which is incorporated herein by reference in its entirety. Expression vectors were found to contain nucleic acid sequences in both the sense and antisense orientations. The presence of known genes, open reading frames, and ribosome binding sites was determined by comparison to public databases holding genetic information and various computer programs such as the Genetics Computer Group
30 programs FRAMES and CODONPREFERENCE. Clones were designated as "antisense" if the cloned fragment was oriented to the promoter such that the RNA transcript produced was complementary to the expressed mRNA from a chromosomal locus. Clones were

designated as "sense" if they coded for an RNA fragment that was identical to a portion of a wild type mRNA from a chromosomal locus.

The sequences described in Examples 1-2 that inhibited bacterial proliferation and contained gene fragments in an antisense orientation are listed in Table I. This table lists each identified sequence by: a sequence identification number; a Molecule Number; a gene to which the identified sequence corresponds, listed according to the National Center for Biotechnology Information (NCBI), Blattner (Science 277:1453-1474(1997); also contains the *E. coli* K-12 genome sequence), or Rudd (Micro. and Mol. Rev. 62:985-1019 (1998)), (both papers are hereby incorporated by reference) nomenclatures. The CONTIG numbers for each identified sequence is shown, as well as the location of the first and last base pairs located on the *E. coli* chromosome. A Molecule Number with a "***" indicates a clone corresponding to an intergenic sequence.

The sequences of the nucleic acid inserts of SEQ ID NOs: 1-81 from U.S. Provisional Patent Application No. 60/117,405 which inhibited proliferation were further analyzed. The reanalyzed sequences corresponding to SEQ ID NOs. 1-81 of U.S. Provisional Patent Application No. 60/117,405 have SEQ ID NOs. 405-485 in the present application.

SEQ ID NOs: 82-242 in U.S. Provisional Patent Application No. 60/117,405 are identical to SEQ ID NOs: 82-242 of the present application with the following exceptions. SEQ ID NO: 148 in the present application is the complementary strand of SEQ ID NO: 148 in U.S. Provisional Patent Application No. 60/117,405. Accordingly, the protein of SEQ ID NO: 308 which is encoded by SEQ ID NO: 148 has also been revised. SEQ ID NO: 163 in the present application is the complementary strand of SEQ ID NO: 163 in U.S. Provisional Patent Application No. 60/117,405. Accordingly, the protein of SEQ ID NO: 323 which is encoded by SEQ ID NO: 163 has also been revised.

The target gene of SEQ ID NOs. 18 and 19 of U.S. Provisional Patent Application No. 60/117,405 (SEQ ID NOs. 18, 19, 422, 423 of the present application) has been revised from *dicF* to *ftsZ* to reflect the fact that these SEQ ID NOs. include natural antisense molecules which inhibit *ftsZ* expression.

The gene products of the nucleic acids of SEQ ID NOs. 198 and 239-242 in U.S. Provisional Patent Application No. 60/117,405 and in the present application (SEQ ID

NOs. 358 and 399-402 of the present application) have been revised to reflect the fact that these nucleic acids encode nontranslated tRNAs and rRNAs. Tables I and II have been revised accordingly. The SEQ ID NOs. in Table II were also revised to reflect the fact that SEQ ID NOs: 89 and 402 were identical in U.S. Provisional Patent Application No. 60/117,405.

TABLE I
Identified Clones with Corresponding Genes and Operons

SEQ ID NO.	Molecule No.	Gene (NCBI)	Gene (Blattner)	Gene (Rudd)	CONTIG
1, 405	EcXA001	<i>yhhQ</i>	<i>b3471</i>	<i>yhhQ</i>	AE000423
2, 406	EcXA002	<i>lepB</i>	<i>lepB</i>	<i>lepB</i>	AE000343
3, 407	EcXA003	<i>f586</i>	<i>b0955</i>	<i>ycbZ</i>	AE000197
4, 408	EcXA004	<i>rpsG, rpsL</i>	<i>b3341</i>	<i>rpsG, rpsL</i>	AE000410
5, 409	EcXA005a	<i>rplL, rplJ</i>	<i>b3986</i>	<i>rplL, rplJ</i>	AE000472
6, 410	EcXA005b	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472
7, 411	EcXA005c	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	AE000472
8, 412	EcXA005d	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	<i>rplL, rplJ</i>	AE000472
9, 413	EcXA005e	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472
10, 414	EcXA005f	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472
11, 415	EcXA005g	<i>rplL</i>	<i>rplL</i>	<i>rplL</i>	AE000472
12, 416	EcXA006	<i>pta</i>	<i>b2297</i>	<i>pta</i>	AE000319
13, 417	EcXA007	<i>yicP</i>	<i>b3666</i>	<i>yicP</i>	AE000444
14, 418	EcXA008a	<i>yhaU</i>	<i>b3127</i>	<i>yhaU</i>	AE000394
15, 419	EcXA008b	<i>yhaU</i>	<i>yhaU</i>	<i>yhaU</i>	AE000394
16, 420	EcXA008c	<i>yhaU</i>	<i>yhaU</i>	<i>yhaU</i>	AE000394
17, 421	EcXA009	<i>ydeY</i>	<i>ydeY</i>	<i>ydeY</i>	AE000249
18, 422	EcXA010a (natural as)	<i>dicF</i>	<i>b1575</i>	<i>dicF</i>	AE000253
19, 423	EcXA010b	<i>dicF</i>	<i>dicF</i>	<i>dicF</i>	AE000253
20, 424	EcXA011	<i>fdnG</i>	<i>b1474</i>	<i>fdnG</i>	AE000244
21, 425	EcXA012a	<i>fusA</i>	<i>b3340</i>	<i>fusA</i>	AE000410
22, 426	EcXA012b	<i>fusA</i>	<i>fusA</i>	<i>fusA</i>	AE000410
23, 427	EcXA012c	<i>fusA</i>	<i>fusA</i>	<i>fusA</i>	AE000410
24, 428	EcXA013a	<i>o86</i>	<i>b2562</i>	<i>yfhL</i>	AE000342
25, 429	EcXA013b	<i>o86</i>	<i>b2562</i>	<i>yfhL</i>	AE000342
26, 430	EcXA013c	<i>o86</i>	<i>b2562</i>	<i>yfhL</i>	AE000342
27, 431	EcXA014	<i>visC</i>	<i>b2906</i>	<i>visC</i>	AE000374
28, 432	EcXA015	<i>yfdI</i>	<i>yfdI</i>	<i>yfdI</i>	AE000323
29, 433	EcXA016	<i>yeaQ</i>	<i>yeaQ</i>	<i>yeaQ</i>	AE000274
		<i>yoaG</i>	<i>yoaG</i>	<i>yoaG</i>	

SEQ ID NO.	Molecule No.	Gene (NCBI)	Gene (Blattner)	Gene (Rudd)	CONTIG
30, 434	EcXA017a	<i>yggE</i>	<i>b2922</i>	<i>yggE</i>	AE000375
31, 435	EcXA017b	<i>yggE</i>	<i>yggE</i>	<i>yggE</i>	AE000375
32, 436	EcXA018a	<i>o464</i>	<i>b2074</i>	<i>yegM</i>	AE000297
33, 437	EcXA018b	<i>o464</i>	<i>b2074</i>	<i>yegM</i>	AE000297
34, 438	EcXA019a	<i>yehA</i>	<i>yehA</i>	<i>yehA</i>	AE000300
					AE000299
35, 439	EcXA019b	<i>o172, yehA</i>	<i>o172, yehA</i>	<i>o172, yehA</i>	AE000299
36, 440	EcXA020	<i>o384, f82</i>	<i>b1794, b1795</i>	<i>yeaP, yeaQ</i>	AE000274
37, 441	EcXA021a	<i>fl12</i>	<i>b0218</i>	<i>yafU</i>	AE000130
38, 442	EcXA021b	<i>fl12</i>	<i>b0218</i>	<i>yafU</i>	AE000130
39, 443	EcXA022	<i>o740</i>	<i>b1629</i>	<i>ydgN</i>	AE000258
40, 444	EcXA023a	<i>fl176, f382</i>	<i>b1504, b1505</i>	<i>ydeS, ydeT</i>	AE000247
41, 445	EcXA023b	<i>fl176, f382</i>	<i>b1504, b1505</i>	<i>ydeS, ydeT</i>	AE000247
42, 446	EcXA024	<i>ygjM, ygjN</i>	<i>b3082</i>	<i>ygjM, ygjN</i>	AE000390
43, 447	EcXA025	<i>O2383</i>	<i>b1878</i>	<i>yeeJ</i>	AE000289
44, 448	EcXA026	<i>o61</i>	Unpre- dicted	Unpre- dicted	AE000138
45, 449	EcXA027a	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
46, 450	EcXA027b	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
47, 451	EcXA027c	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
		<i>yohI</i>	<i>yohI</i>	<i>yohI</i>	
48, 452	EcXA027d	<i>yohH</i>	<i>yohH</i>	<i>yohH</i>	AE000303
49, 453	EcXA028	<i>f296</i>	<i>b2305</i>	<i>yfcI</i>	AE000319
50, 454	EcXA029	<i>yjjK</i>	<i>b4391</i>	<i>yjjK</i>	AE000509
51, 455	EcXA030	<i>yi5A</i>	<i>b3557</i>	<i>yi5A</i>	AE000433
52, 456	EcXA031	<i>rplE</i>	<i>B3308</i>	<i>rplE</i>	AE000408
53, 457	EcXA032a	<i>ybgD</i>	<i>ybgD</i>	<i>ybgD</i>	AE000175
54, 458	EcXA032b **	<i>ybgD</i>	<i>ybgD</i>	<i>ybgD</i>	AE000175
		<i>gltA</i>	<i>gltA</i>	<i>gltA</i>	
55, 459	EcXA033a	<i>f477 (as)</i>	<i>b3052</i>	<i>waaE</i>	AE000387
					AE000386
56, 460	EcXA033b	<i>f477</i>	<i>b3052</i>	<i>waaE</i>	AE000387
57, 461	EcXA034a	<i>cspA</i>	<i>b3556</i>	<i>cspA</i>	AE000433
58, 462	EcXA034b	<i>cspA</i>	<i>b3556</i>	<i>cspA</i>	AE000433
59, 463	EcXA035	<i>yhjU</i>	<i>yhjU</i>	<i>yhjU</i>	AE000431
60, 464	EcXA036	<i>yqjF</i>	<i>b3101</i>	<i>yqjF</i>	AE000392
		<i>o99</i>	<i>b3100,</i>	<i>yqjK</i>	
61, 465	EcXA037	<i>ydeH</i>	<i>b1535</i>	<i>ydeH</i>	AE000251

SEQ ID NO.	Molecule No.	Gene (NCBI)	Gene (Blattner)	Gene (Rudd)	CONTIG
62, 466	EcXA038	<i>sieB</i>	<i>b1353</i>	<i>sieB</i>	AE000233
63, 467	EcXA039	<i>ybbD</i>		<i>ybbD</i>	AE000156
64, 468	EcXA040	<i>InsB_6</i>	<i>b3445</i>	<i>insB_6</i>	AE000420
65, 469	EcXA041	<i>f234</i>	<i>b1138</i>	<i>ymfE</i>	AE000214
66, 470	EcXA042a	<i>rplY</i>	<i>rplY</i>	<i>rplY</i>	AE000308
67, 471	EcXA042b	<i>rplY</i>	<i>rplY</i>	<i>rplY</i>	AE000308
68, 472	EcXA043	<i>ybgB</i>	<i>ybgB</i>	<i>ybgB</i>	AE000176
		<i>cydA</i>	<i>cydA</i>	<i>cydA</i>	
69, 473	EcXA044	<i>purB</i>	<i>b1131</i>	<i>purB</i>	AE000213
70, 474	EcXA045* *	<i>csrA</i>	<i>csrA</i>	<i>csrA</i>	AE000353
		<i>serV</i>	<i>serV</i>	<i>serV</i>	
71, 475	EcXA046* *	<i>fimE, fimA</i>	<i>b4313</i>	<i>fimE, fimA</i>	AE000502
72, 476	EcXA047* *	<i>f96, cspB</i>	<i>f96, cspB</i>	<i>cspB, ydfS</i>	AE000252
73, 477	EcXA048	<i>yefE</i>	<i>yefE</i>	<i>yefE</i>	AE000294
74, 478	EcXA049	<i>yaiC</i>	<i>b0385</i>	<i>yaiC</i>	AE000145
75, 479	EcXA050	<i>o467, o222</i>	<i>yaiU, yaiV</i>	<i>yaiU, yaiV</i>	AE000144
76, 480	EcXA051a	<i>rplB, rplW</i>	<i>rplB, rplW</i>	<i>rplB, rplW</i>	AE000408
77, 481	EcXA051b	<i>rplW</i>	<i>rplW</i>	<i>rplW</i>	AE000408
78, 482	EcXA052	<i>infC</i>	<i>infC</i>	<i>infC</i>	AE000267
					AE000266
79, 483	EcXA053	<i>gor</i>	<i>gor</i>	<i>gor</i>	AE000426
80, 484	EcXA054	<i>rplF</i>	<i>rplF</i>	<i>rplF</i>	AE000408
81, 485	EcXA055	<i>rrlG</i>	<i>rrlG</i>	<i>rrlG</i>	AE000345

EXAMPLE 4

Identification of Genes and their Corresponding Operons Affected by Antisense Inhibition

The sequencing of the entire E. coli genome is described in Blattner et al., Science 277:1453-1474(1997) the entirety of which is hereby incorporated by reference and the sequence of the genome is listed in GenBank Accession No.U00096, the disclosure of which is incorporated herein by reference in its entirety. The operons to which the proliferation-inhibiting nucleic acids correspond were identified using RegulonDB and information in the literature. The coordinates of the boundaries of these operons on the E. coli genome are listed in Table III. Table II lists the molecule numbers of the inserts containing the growth inhibiting nucleic acid fragments, the genes in the operons

corresponding to the inserts, the SEQ ID NOs of the genes containing the inserts, the SEQ ID NOs of the proteins encoded by the genes, the start and stop points of the genes on the E. coli genome, the orientation of the genes on the genome, whether the operons are predicted or documented, and the predicted functions of the genes. The identified operons, their putative functions, and whether or not the genes are presently thought to be required for proliferation are discussed below.

Functions for the identified genes were determined by using either Blattner functional class designations or by comparing identified sequence with known sequences in various databases. A variety of biological functions were noted for the genes to which the clones of the present invention correspond. The functions for the genes of interest appear in Table II.

The proteins that are listed in Table II are involved in a wide range of biological functions.

TABLE II

All Operon Data with Whole Chromosome Coordinates

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
82	243	EcXA001	<i>yhhQ</i>	3606848	3607513	(P)	Hypothetical ORF, unclassified, unknown	Hypothetical outer membrane protein
83	244		<i>dcrB</i>	3607532	3608143		Hypothetical ORF, unclassified, unknown	Resistance to phage C1; periplasmic protein perhaps anchored to inner membrane
84	245	EcXA002	<i>lepB</i>	2702355	2703329	(P)	Transport and binding proteins	Secretion
85	246	EcXA003	<i>yebZ</i>	1015762	1017522	(P)	Unknown	Protease
86	247	EcXA004	<i>tufA</i>	3467782	3468966	(D)	Translation, post-translational modification	Translation (Elongation factor Tu)
87	248		<i>fusA</i>	3469037	3471151		Translation, post-translational modification	Translation (elongation factor efg)
88	249		<i>rpsG</i>	3471179	3471718		Translation, post-translational modification	Translation

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
89	402	EcXA055	<i>rrsG</i>	2727636	2729178		Translation, post-translational modification	Translation (rRNA)
90	250		<i>rpsL</i>	3471815	3471815		Translation, post-translational modification	Translation
91	251	EcXA005a-g	<i>rplJ</i>	4177574	4178071	(D)	Translation, post-translational modification	Translation
92	252		<i>rplL</i>	4178138	4178503		Translation, post-translational modification	Translation
93	253	EcXA006	<i>pta</i>	2412767	2414911	(P)	Carbon compound catabolism	Carbon compound catabolism
94	254	EcXA007	<i>yicP</i>	3841591	3843357	(P)	Hypothetical ORF, unclassified, unknown	Probable adenine deaminase
95	255	EcXA008a-c	<i>yhaD</i>	3268266	3269492	(P)	Hypothetical ORF, unclassified, unknown	
96	256		<i>yhaE</i>	3269508	3270407		Putative enzymes	
97	257		<i>yhaF</i>	3270428	3271198		Hypothetical ORF, unclassified, unknown	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
								genase)
107	267		<i>fhnH</i>	1548485	1549369		Energy metabolism	
108	268		<i>fhnI</i>	1549362	1550015		Energy metabolism	
		EcXA 012a-c	Same operon as EcXA004					
109	269	EcXA013a-c	<i>yhlL</i>	2697683	2697943	(P)	Hypothetical ORF, unclassified, unknown	No homologues, no motifs
110	270	EcXA014	<i>visC</i>	3049135	3050337	(P)	Hypothetical ORF, unclassified, unknown	Ubiquinone synthesis
111	271		<i>ubiH</i>	3050360	3051538		Biosynthesis of cofactors, prosthetic groups and carriers	
112	272		<i>pepP</i>	3051535	3052860		Translation, post-translational modification	
113	273		<i>ygfB</i>	3052886	3053470		Hypothetical ORF, unclassified, unknown	
114	274	EcXA015	<i>yfdG</i>	2465875	2466237	(P)	Hypothetical ORF, unclassified, unknown	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
115	275		<i>yfdH</i>	2466234	2467154		Cell structure	
116	276		<i>yfdI</i>	2467151	2468482		Hypothetical ORF, unclassified, unknown	Putative membrane protein
117	277	EcXA016	<i>yeaQ</i>	1877031	1877279	(P)	Hypothetical ORF, unclassified, unknown	Homologue to transgly-cosylase associated protein
118	278		<i>yoaG</i>	1877427	1877609	(P)	Hypothetical ORF, unclassified, unknown	No homologues
119	279		<i>yeaR</i>	1877613	1877972		Hypothetical ORF, unclassified, unknown	
120	280	EcXA017a-b	<i>yggE</i>	3065360	3066100	(P)	Structural proteins	Homologues in multiple bacteria, no motifs
121	281	EcXA018a-b	<i>yegM</i>	2151891	2153285	(P)	Putative transport proteins	Transport (multiple transferable resistance)
122	282		<i>yegN</i>	2153285	2156407		Hypothetical ORF, unclassified, unknown	
123	283		<i>yegO</i>	2156408	2159485		Hypothetical ORF, unclassified, unknown	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
124	284		<i>yegB</i>	2159486	2160901		Putative transport proteins	
125	285	EcXA019a-b	<i>yehA</i>	2185400	2186434	(P)	Cell structure	Weak homology to pilin precursor from <i>H. Inf.</i>
126	286		<i>yehB</i>	2186450	2188930		Hypothetical ORF, unclassified, unknown	
127	287		<i>yehC</i>	2188946	2189665		Putative chaperones	
128	288		<i>yehD</i>	2189700	2190242		Cell structure	
		EcXA020	Same operon as EcXA016 (one of the two)					
129	289	EcXA021a-b	<i>yafU</i>	238746	239084	(P)	Hypothetical ORF, unclassified, unknown	Homologues in <i>H. Inf.</i> and <i>S. Pombe.</i> , no motifs, transmembrane region present
130	290	EcXA022	<i>ydgL</i>	1703791	1704372	(P)	Hypothetical ORF, unclassified, unknown	
131	291		<i>ydgM</i>	1704372	1704950		Hypothetical ORF, unclassified, unknown	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
132	292		<i>ydgN</i>	1704943	1707165		Hypothetical ORF, unclassified, unknown	
133	293		<i>ydgO</i>	1707166	1708224		Hypothetical ORF, unclassified, unknown	
134	294		<i>ydgP</i>	1708228	1708848		Hypothetical ORF, unclassified, unknown	
135	295		<i>ydgQ</i>	1708852	1709547		Hypothetical ORF, unclassified, unknown	
136	296		<i>nth</i>	1709547	1710182		Transcription, RNA processing and degradation	
137	297	EcXA023a-b	<i>ydeR</i>	1585817	1586320	(P)	Hypothetical ORF, unclassified, unknown	
138	298		<i>ydeS</i>	1586333	1586863		Hypothetical ORF, unclassified, unknown	fimf-like
139	299		<i>ydeT</i>	1586877	1588025		Structural proteins	fimf-like
140	300	EcXA024	<i>ygiM</i>	3231369	3231785	(P)	Hypothetical ORF, unclassified, unknown	Weak homology to long chain fatty acid coa ligase in

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
								Archaeoglobus
141	301		<i>ygiN</i>	3231782	3232096		Hypothetical ORF, unclassified, unknown	Homologues in various bacteria
142	302	EcXA025	<i>yeeJ</i>	2042885	2050036	(P)	Hypothetical ORF, unclassified, unknown	Strong similarity to numerous attaching and effacing proteins and invasins
143	303	EcXA026	<i>rajA</i>	331001	331184	unpredicted		nifm like
144	304	EcXA027a-d	<i>yohG</i>	2225343	2226539	(P)	Putative transport proteins	
145	305		<i>yohH</i>	2226569	2226859		Hypothetical ORF, unclassified, unknown	Xylose binding protein-like
146	306		<i>yohI</i>	2227458	2228405	(P)	Putative regulatory protein	
147	307	EcXA028	<i>ycfI</i>	2420669	2421559	(P)	Hypothetical ORF, unclassified, unknown	Similar to <i>S. Typhi</i> histidine transport gene
148	308	EcXA029	<i>yjiK</i>	4626424	4628091	(P)	Hypothetical ORF, unclassified, unknown	Similar to ABC transporter

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
149	309	EcXA030	<i>yi5A</i>	3718309	3718830	(P)	Hypothetical ORF, unclassified, unknown	IS150 orf A
150	310		<i>yi5B</i>	3718827	3719678		Phage, transposon, or plasmid	
151	311	EcXA031	<i>rpmJ</i>	3440255	3440371	(D)	Translation, post-translational modification	
152	312		<i>prlA</i>	3440403	3441734		Putative transport proteins	
153	313		<i>rplO</i>	3441742	3442176		Translation, post-translational modification	
154	314		<i>rpmD</i>	3442180	3442359		Translation, post-translational modification	
155	315		<i>rpsE</i>	3442363	3442866		Translation, post-translational modification	
156	316		<i>rplR</i>	3442881	3443234		Translation, post-translational modification	
157	317		<i>rplF</i>	3443244	3443777		Translation, post-translational modification	Translation

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
158	318		<i>rpsH</i>	3443790	3444182		Translation, post-translational modification	
159	319		<i>rpsN</i>	3444216	3444521		Translation, post-translational modification	
160	320		<i>rplE</i>	3444536	3445075		Translation, post-translational modification	Translation
161	321		<i>rplX</i>	3445090	3445404		Translation, post-translational modification	
162	322		<i>rplN</i>	3445415	3445786		Translation, post-translational modification	
163	323	EcXA032a-b	<i>ybgD</i>	751452	752018	(P)	Cell processes (incl. Adaptation, protection)	Hypothetical fimbrial protein
164	324		<i>gltA</i>	752408	753691	(D)	Energy metabolism	Glutamine biosynthesis
165	325	EcXA033a-b	<i>waaE</i>	3192961	3194394	(P)	Putative enzymes	ADP heptose synthase/ autotrophic growth protein
166	326		<i>glnE</i>	3194442	3197282		Translation, post-translational	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
							modification	
167	327		<i>ygiF</i>	3197305	3198606		Hypothetical ORF, unclassified, unknown	
168	328	EcXA034a-b	<i>cspA</i>	3717678	3717890	(P)	Cell processes (incl. Adaptation, protection)	RNA chaperonin
169	329	EcXA035	<i>yhjS</i>	3694087	3695658	(P)	Translation, post-translational modification	
170	330		<i>yhjT</i>	3695658	3695846		Hypothetical ORF, unclassified, unknown	
171	331		<i>yhjU</i>	3695843	3697522		Hypothetical ORF, unclassified, unknown	Regions similar to dehydro-genases, nucleases etc.
172	332	EcXA036	<i>yqjC</i>	3246594	3246977	(P)	Hypothetical ORF, unclassified, unknown	
173	333		<i>yqjD</i>	3247015	3247320		Hypothetical ORF, unclassified, unknown	
174	334		<i>yqjE</i>	3247323	3247727		Hypothetical ORF, unclassified,	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
							unknown	
175	335		<i>yqjK</i>	3247717	3248016		Similar to mukb from H. Inf.	
176	336		<i>yqjF</i>	3248112	3248594	(P)	Hypothetical ORF, unclassified, unknown	Homologues in many bacteria, blocks; secretion/ ATP synthase/ftsZ
177	337	EcXA037	<i>ydeH</i>	1620984	1621874	(P)	Hypothetical ORF, unclassified, unknown	Similar to carboxy-kinase, oxidase, symporters
178	338	EcXA038	<i>sieB</i>	1416572	1417183	(P)	Phage, transposon, or plasmid	Super-infection exclusion factor B-like
179	339		<i>rajB</i> (b1354)	1417192	1417368		Hypothetical ORF, unclassified, unknown	
180	340	EcXA039	<i>rhdD</i>	522485	526765	(P)	Hypothetical ORF, unclassified, unknown	
181	341		<i>ybbC</i>	526805	527173		Hypothetical ORF, unclassified, unknown	
182	342		<i>ylbH</i>	527173	527883		Hypothetical ORF, unclassified,	Rhs-like element

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
							unknown	
183	343		<i>ybbD</i>	527864	528124		Hypothetical ORF, unclassified, unknown	ATP synthase, desaturase
184	344		<i>yblI</i>	528163	528354		Hypothetical ORF, unclassified, unknown	
185	345	EcXA040	<i>insB_6</i>	351114	351389	(P)	Phage, transposon, or plasmid	
186	346		<i>insA</i>	351308	3581811		Phage, transposon, or plasmid	
187	347		<i>yrhA</i>	3580669	3581085		Hypothetical ORF, unclassified, unknown	
188	348		<i>yhhZ</i>	3579494	3580672		Hypothetical ORF, unclassified, unknown	
189	349	EcXA041	<i>ymfD</i>	1196090	1196755	(P)	Hypothetical ORF, unclassified, unknown	No assigned role
190	350		<i>ymfE</i>	1196756	1197460		Hypothetical ORF, unclassified, unknown	No assigned role

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
191	351	EcXA042a-b	<i>rplY</i>	2280537	2280821	(P)	Translation, post-translational modification	Translation
192	352	EcXA043	<i>hrsA</i>	765207	767183	(P)	Translation, post-translational modification	
193	353		<i>ybgB</i>	767201	769834		Carbon compound catabolism	Unknown
194	354		<i>cydA</i>	770678	772249	(D)	Energy metabolism	Cytochrome D oxidase
195	355		<i>cydB</i>	772265	773404		Energy metabolism	
196	356	EcXA044	<i>purB</i>	1189839	1191209	(D)	Nucleotide biosynthesis and metabolism	Purine biosynthesis
197	357	EcXA045	<i>csrA</i>	2816983	2817168	(P)	Regulatory function	Carbon storage regulator (mRNA decay factor)
198	358		<i>serV</i>	2816575	2816667	Unpredicted	Translation, post-translational modification	Translation (tRNA)
199	359	EcXA046	<i>fimB</i>	4538525	4539127	(D)	Cell structure	
200	360		<i>fimE</i>	4539605	4540201		Cell structure	Fimbriae
201	361		<i>fimA</i>	4540683	4541231		Cell structure	Regulator of inversion
202	362		<i>fimI</i>	4541188	4541835		Cell structure	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
203	363		<i>fimC</i>	4541872	4542597		Cell structure	
204	364		<i>fimD</i>	4542665	4545301		Cell structure	
205	365		<i>fimF</i>	4545311	4545841		Cell structure	
206	366		<i>fimG</i>	4545854	4546357		Cell structure	
207	367		<i>fimH</i>	4546377	4547279		Cell structure	
208	368	EcXA047	<i>ydfP</i>	1637054	1638684	(P)	Hypothetical ORF, unclassified, unknown	
209	369		<i>ydfQ</i>	1637548	1638081		Hypothetical ORF, unclassified, unknown	
210	370		<i>ydfR</i>	1638078	1638389		Hypothetical ORF, unclassified, unknown	
211	371		<i>ydfS</i>	1638394	1638684		Hypothetical ORF, unclassified, unknown	Lysis protein
212	372		<i>cspB</i>	1639363	1639578	(P)	Cell processes (incl. Adaptation, protection)	
213	373	EcXA048	<i>yi52_7</i>	2099917	2100933	(P)	Phage, transposon, or plasmid	
214	374		<i>yefJ</i>	2100938	2101411		Putative enzymes	
215	375		<i>yefI</i>	2101413	2102531		Hypothetical ORF, unclassified,	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
							unknown	
216	376		<i>yefH</i>	2102516	2103106		Putative enzymes	
217	377		<i>yefG</i>	2103087	2104079		Hypothetical ORF, unclassified, unknown	
218	378		<i>rfc</i>	2104082	2105248		Cell structure	
219	379		<i>yefE</i>	2105248	2106351		Hypothetical ORF, unclassified, unknown	UDP galacto-pyranase mutase
220	380	EcXA049	<i>yaiC</i>	402927	404042	(P)	Hypothetical ORF, unclassified, unknown	Unknown
221	381	EcXA050	<i>yaiU</i>	392239	393642	(P)	Putative enzymes	Putative auto-transporter
222	382		<i>yaiV</i>	393685	394353		Hypothetical ORF, unclassified, unknown	Hypothetical outer membrane protein
223	383	EcXA051a-b	<i>rpsQ</i>	3445951	3446205	(D)	Translation, post-translational modification	
224	384		<i>rpmC</i>	3446205	3446396		Translation, post-translational modification	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
225	385		<i>rplP</i>	3446396	3446806		Translation, post-translational modification	
226	386		<i>rpsC</i>	3446819	3447520		Translation, post-translational modification	
227	387		<i>rplV</i>	3447538	3447870		Translation, post-translational modification	
228	388		<i>rpsS</i>	3447885	3448163		Translation, post-translational modification	
229	389		<i>rplB</i>	3448180	3449001		Translation, post-translational modification	Translation
230	390		<i>rplW</i>	3449019	3449321		Translation, post-translational modification	Translation
231	391		<i>rplD</i>	3449318	3449923		Translation, post-translational modification	
232	392		<i>rplC</i>	3449934	3450563		Translation, post-translational modification	

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
233	393		<i>rpsJ</i>	3450596	3450907		Translation, post-translational modification	
234	394	EcXA052	<i>rpIT</i>	1797417	1797773	(D)	Translation, post-translational modification	
235	395		<i>rpml</i>	1797826	1798023		Translation, post-translational modification	
236	396		<i>infC</i>	1798120	1798662		Translation, post-translational modification	Translation
237	397		<i>thrS</i>	1798666	1800594		Translation, post-translational modification	
238	398	EcXA053	<i>gor</i>	3643929	3645281	(P)	Biosynthesis of cofactors, prosthetic groups and carriers	Glutathione oxidoreductase
		EcXA054	Same operon as EcXA031					
239	399	EcXA055	<i>rrlG</i>	2724301	2727204	(D)	Translation, post-translational modification	Translation (rRNA)

GeneSeq ID No.	Gene Prod. Seq ID No.	Mole. No.	Genes On Operon	Left Coordinate	Right Coordinate	Predicted (P) Or Documented (D) Operon	Blattner functional class of encoded proteins	Predicted functional class of encoded proteins
240	400		<i>rrfG</i>	2724089	2724208		Translation, post-translational modification	Translation (rRNA)
241	401		<i>gltW</i>	2727389	2727464		Translation, post-translational modification	Translation (tRNA)
242	402		<i>rrsG</i>	2727636	2729178		Translation, post-translational modification	Translation (rRNA)

Several of the expression vectors contain fragments that correspond to genes of unknown function or if the function is known, it is not known whether the gene is essential. For example, EcXA001, 003, 007, 008, 013, 015, 016, 017, 018, 019, 020, 021, 022, 023, 024, 025, 026, 027, 028, 029, 030, 032, 033, 034, 035, 036, 037, 038, 039, 040, 041, 047, 048, 049 and 050 are all exogenous nucleic acid sequences that correspond to *E. coli* proteins that have no known function or where the function has not been shown to be essential or nonessential.

The present invention reports a number of novel *E. coli* genes and operons that are required for proliferation. From the list clone sequences identified here, each was identified to be a portion of a gene in an operon required for the proliferation of *E. coli*. Cloned sequences corresponding to genes already known to be required for proliferation in *E. coli* include EcXA002, 004, 005, 010, 012, 014, 031, 02, 043, 045, 051, 052, 054, and 055. The remaining identified sequences correspond to *E. coli* genes previously undesignated as required for proliferation in the art.

An interesting observation of the present invention is that there are also several sequence fragments that correspond to *E. coli* genes that are not thought to be required for *E. coli* proliferation. Nevertheless, under the conditions described above, the antisense expression of these gene fragments causes a reduction in cell growth. This result implies that the genes corresponding to the identified sequences are actually required for proliferation. Molecule Nos. corresponding to these genes are EcXA006, 044, 046, and 053.

Following identification of the sequences of interest, these sequences were localized into operons. Since bacterial genes are expressed in a polycistronic manner, the antisense inhibition of a single gene in an operon might effect the expression of all the other genes on the operon or the genes down stream from the single gene identified. In order to determine which of the gene products in an operon are required for proliferation, each of the genes contained within an operon may be analyzed for their effect on viability as described below.

TABLE III

Operon Boundaries

Mole. No.	Left Coordinate	Right Coordinate
EcXA001	3606848	3608143
EcXA002	2702355	2703329
EcXA003	1015762	1017522
EcXA004	3467782	3472189
EcXA005	4177574	4178503
EcXA006	2412767	2414911
EcXA007	3841591	3843357
EcXA008	3268266	3272548
EcXA009	1599514	1605313
EcXA010	1647406	1647458
EcXA011	1545425	1550015
EcXA012	3467782	3472189
EcXA013	2697683	2697943
EcXA014	3049135	3053470
EcXA015	2465875	2468482
EcXA016	1877031	1877972
EcXA017	3065360	3066100
EcXA018	2151891	2160901
EcXA019	2185400	2190242
EcXA020	1877031	1877972
EcXA021	238746	239084
EcXA022	1703791	1710182
EcXA023	1585817	1588025
EcXA024	3231369	3232096
EcXA025	2042885	2050036
EcXA026	331001	331184
EcXA027c	2225343	2228405
EcXA028	2420669	2421559
EcXA029	4626424	4628091
EcXA030	3718309	3719678
EcXA031	3440255	3445786
EcXA032b	751452	753691
EcXA033	3192961	3198606
EcXA034	3717678	3717890
EcXA035	3694087	3697522
EcXA036	3246594	3248594
EcXA037	1620984	1621874
EcXA038	1416572	1417368
EcXA039	522485	528354
EcXA040	3580669	3580672
EcXA041	1196090	1197460

Mole. No.	Left Coordinate	Right Coordinate
EcXA042	2280537	2280821
EcXA043	765207	773404
EcXA044	1189839	1191209
EcXA045	2816575	2817168
EcXA046	4538525	4547279
EcXA047	1637054	1639578
EcXA048	2099917	2106351
EcXA049	402927	404042
EcXA050	392239	394353
EcXA051	3445951	3450907
EcXA052	1797417	1800594
EcXA053	3643929	3645281
EcXA054	3440255	3445786
EcXA055	2724301	2729178

EXAMPLE 5

Identification of Individual Genes within an Operon Required for Proliferation

The following example illustrates a method for determining which gene in an operon is required for proliferation. The clone insert corresponding to Molecule No. EcXA004 possesses nucleic acid sequence homology to the *E. coli* genes *rspG* and *rspL*. This molecule corresponds to an operon containing two additional genes *fusA* and *tufA*. The *rpsL* gene is the first gene in the operon. To determine which gene or genes in this operon are required for proliferation, each gene is selectively inactivated using homologous recombination. Gene *rpsL* is the first gene to be inactivated.

Deletion inactivation of a chromosomal copy of a gene in *E. coli* can be accomplished by integrative gene replacement. The principle of this method (Hamilton, C. M., et al 1989. *J. Bacteriol.* 171: 4617-4622) is to construct a mutant allele of the targeted gene, introduce that allele into the chromosome using a conditional suicide vector, and then force the removal of the native wild type allele and vector sequences. This will replace the native gene with a desired mutation(s) but leave promoters, operators, etc. intact. Essentiality of a gene is determined either by deduction from genetic analysis or by conditional expression of a wild type copy of the targeted gene (trans complementation).

The first step is to generate a mutant *rpsL* allele using PCR amplification. Two sets of PCR primers are chosen to produce a copy of *rpsL* with a large central deletion

to inactivate the gene. In order to eliminate polar effects, it is desirable to construct a mutant allele comprising an in-frame deletion of most or all of the coding region of the *rpsL* gene. Each set of PCR primers is chosen such that a region flanking the gene to be amplified is sufficiently long to allow recombination (typically at least 500 nucleotides on each side of the deletion). The targeted deletion or mutation will be contained within this fragment. To facilitate cloning of the PCR product, the PCR primers may also contain restriction endonuclease sites found in the cloning region of a conditional knockout vector such as pKO3 (Link, et al 1997 *J. Bacteriol.* **179** (20): 6228-6237). Suitable sites include NotI, SalI, BamHI and SmaI. The *rpsL* gene fragments are produced using standard PCR conditions including, but not limited to, those outlined in the manufacturers directions for the Hot Start Taq PCR kit (Qiagen, Inc., Valencia, CA). The PCR reactions will produce two fragments that can be fused together. Alternatively, crossover PCR can be used to generate a desired deletion in one step (Ho, S. N., et al 1989. *Gene* **77**: 51-59, Horton, R. M., et al 1989. *Gene* **77**: 61-68). The mutant allele thus produced is called a "null" allele because it cannot produce a functional gene product.

The mutant allele obtained from PCR amplification is cloned into the multiple cloning site of pKO3. Directional cloning of the *rpsL* null allele is not necessary. The pKO3 vector has a temperature-sensitive origin of replication derived from pSC101. Therefore, clones are propagated at the permissive temperature of 30°C. The vector also contains two selectable marker genes: one that confers resistance to chloramphenicol and another, the *Bacillus subtilis* *sacB* gene, that allows for counter-selection on sucrose containing growth medium. Clones that contain vector DNA with the null allele inserted are confirmed by restriction endonuclease analysis and DNA sequence analysis of isolated plasmid DNA. The plasmid containing the *rpsL* null allele insert is known as a knockout plasmid.

Once the knockout plasmid has been constructed and its sequence verified, it is transformed into a Rec⁺ *E. coli* host cell. Transformation can be by any standard method such as electroporation. In some fraction of the transformed cells, plasmids will integrate into the *E. coli* chromosome by homologous recombination between the *rpsL* null allele in the plasmid and the *rpsL* gene in the chromosome. Transformant colonies in which such an event has occurred are readily selected by growth at the non-

permissive temperature of 43°C and in the presence of chloramphenicol. At this temperature, the plasmid will not replicate as an episome and will be lost from cells as they grow and divide. These cells are no longer resistant to chloramphenicol and will not grow when it is present. However, cells in which the knockout plasmid has integrated into the *E. coli* chromosome remain resistant to chloramphenicol and propagate.

Cells containing integrated knock-out plasmids are usually the result of a single crossover event that creates a tandem repeat of the mutant and native wild type alleles of *rpsL* separated by the vector sequences. A consequence of this is that *rpsL* will still be expressed in these cells. In order to determine if the gene is essential for growth, the wild type copy must be removed. This is accomplished by selecting for plasmid excision, a process in which homologous recombination between the two alleles results in looping out of the plasmid sequences. Cells that have undergone such an excision event and have lost plasmid sequences including *sacB* gene are selected for by addition of sucrose to the medium. The *sacB* gene product converts sucrose to a toxic molecule. Thus counter selection with sucrose ensures that plasmid sequences are no longer present in the cell. Loss of plasmid sequences is further confirmed by testing for sensitivity to chloramphenicol (loss of the chloramphenicol resistance gene). The latter test is important because occasionally a mutation in the *sacB* gene can occur resulting in a loss of *sacB* function with no effect on plasmid replication (Link, et. al., 1997 *J. Bacteriol.* **179** (20): 6228-6237). These artifact clones retain plasmid sequences and are therefore still resistant to chloramphenicol.

In the process of plasmid excision, one of the two *rpsL* alleles is lost from the chromosome along with the plasmid DNA. In general, it is equally likely that the null allele or the wild type allele will be lost. Therefore, if the *rpsL* gene is not essential, half of the clones obtained in this experiment will have the wild type allele on the chromosome and half will have the null allele. However, if the *rpsL* gene is essential, cells containing the null allele will not be obtained as a single copy of the null allele would be lethal.

To determine the essentiality of *rpsL*, a statistically significant number of the resulting clones, at least 20, are analyzed by PCR amplification of the *rpsL* gene. Since the null allele is missing a significant portion of the *rpsL* gene, its PCR product is

significantly shorter than that of the wild type gene and the two are readily distinguished by gel electrophoretic analysis. The PCR products may also be subjected to sequence determination for further confirmation by methods well known to those in the art.

5 The above experiment is generally adequate for determining the essentiality of a gene such as *rpsL*. However, it may be necessary or desirable to more directly confirm the essentiality of the gene. There are several methods by which this can be accomplished. In general, these involve three steps: 1) construction of an episome containing a wild type allele, 2) isolation of clones containing a single chromosomal copy of the mutant null allele as described above but in the presence of the episomal wild type allele, and then 3) determining if the cells survive when the expression of the episomal allele is shut off. In this case, the trans copy of wild type *rpsL* is made by PCR cloning of the entire coding region of *rpsL* and inserting it in the sense orientation downstream of an inducible promoter such as the *E. coli lac* promoter. Transcription of this allele of *rpsL* will be induced in the presence of IPTG which inactivates the *lac* repressor. Under IPTG induction *rpsL* protein will be expressed as long as the recombinant gene also possesses a ribosomal binding site, also known as a “Shine-Dalgarno Sequence”. The trans copy of *rpsL* is cloned on a plasmid that is compatible with pSC101. Compatible vectors include p15A, pBR322, and the pUC plasmids, among others. Replication of the compatible plasmid will not be temperature-sensitive. The entire process of integrating the null allele of *rpsL* and subsequent plasmid excision is carried out in the presence of IPTG to ensure the expression of functional *rpsL* protein is maintained throughout. After the null *rpsL* allele is confirmed as integrated on the chromosome in place of the wild type *rpsL* allele, then IPTG is withdrawn and expression of functional *rpsL* protein shut off. If the *rpsL* gene is essential, cells will cease to proliferate under these conditions. However, if the *rpsL* gene is not essential, cells will continue to proliferate under these conditions. In this experiment, essentiality is determined by conditional expression of a wild type copy of the gene rather than inability to obtain the intended chromosomal disruption.

30 An advantage of this method over some other gene disruption techniques is that the targeted gene can be deleted or mutated without the introduction of large segments of foreign DNA. Therefore, polar effects on downstream genes are eliminated or

minimized. There are methods described to introduce inducible promoters upstream of potential essential bacterial genes. However in such cases, polarity from multiple transcription start points can be a problem. One way of preventing this is to insert a gene disruption cassette that contains strong transcriptional terminators upstream of the integrated inducible promoter (Zhang, Y, and Cronan, J. E. 1996 *J. Bacteriol.* **178** (12): 3614-3620). The described techniques will all be familiar to one of ordinary skill in the art.

Following the analysis of the *rpsL* gene, the other genes of the operon are investigated to determine if they are required for proliferation.

EXAMPLE 6

Expression of the Proteins Encoded by Genes Identified as Required for *E. coli* Proliferation

The following is provided as one exemplary method to express the proliferation-required proteins encoded by the identified sequences described above. First, the initiation and termination codons for the gene are identified. If desired, methods for improving translation or expression of the protein are well known in the art. For example, if the nucleic acid encoding the polypeptide to be expressed lacks a methionine codon to serve as the initiation site, a strong Shine-Delgarno sequence, or a stop codon, these sequences can be added. Similarly, if the identified nucleic acid sequence lacks a transcription termination signal, this sequence can be added to the construct by, for example, splicing out such a sequence from an appropriate donor sequence. In addition, the coding sequence may be operably linked to a strong promoter or an inducible promoter if desired. The identified nucleic acid sequence or portion thereof encoding the polypeptide to be expressed is obtained by PCR from the bacterial expression vector or genome using oligonucleotide primers complementary to the identified nucleic acid sequence or portion thereof and containing restriction endonuclease sequences for *NcoI* incorporated into the 5' primer and *BglII* at the 5' end of the corresponding 3'-primer, taking care to ensure that the identified nucleic acid sequence is positioned in frame with the termination signal. The purified fragment obtained from the resulting PCR reaction is digested with *NcoI* and *BglII*, purified and ligated to an expression vector.

The ligated product is transformed into DH5 α or some other *E. coli* strain suitable for the over expression of potential proteins. Transformation protocols are well known in the art. For example, transformation protocols are described in: **Current Protocols in**

Molecular Biology, Vol. 1, Unit 1.8, (Ausubel, et al., Eds.) John Wiley & Sons, Inc. (1997). Positive transformants are selected after growing the transformed cells on plates containing 50-100 µg/ml Ampicillin (Sigma, St. Louis, Missouri). In one embodiment, the expressed protein is held in the cytoplasm of the host organism. In an alternate
5 embodiment, the expressed protein is released into the culture medium. In still another alternative, the expressed protein can be sequestered in the periplasmic space and liberated therefrom using any one of a number of cell lysis techniques known in the art. For example, the osmotic shock cell lysis method described in Chapter 16 of **Current Protocols in Molecular Biology**, Vol. 2, (Ausubel, et al., Eds.) John Wiley & Sons, Inc.
10 (1997). Each of these procedures can be used to express a proliferation-required protein.

Expressed proteins, whether in the culture medium or liberated from the periplasmic space or the cytoplasm, are then purified or enriched from the supernatant using conventional techniques such as ammonium sulfate precipitation, standard chromatography, immunoprecipitation, immunochromatography, size exclusion
15 chromatography, ion exchange chromatography, and HPLC. Alternatively, the secreted protein can be in a sufficiently enriched or pure state in the supernatant or growth media of the host to permit it to be used for its intended purpose without further enrichment. The purity of the protein product obtained can be assessed using techniques such as Coomassie or silver staining or using antibodies against the control protein. Coomassie and silver
20 staining techniques are familiar to those skilled in the art.

Antibodies capable of specifically recognizing the protein of interest can be generated using synthetic peptides using methods well known in the art. See, **Antibodies: A Laboratory Manual**, (Harlow and Lane, Eds.) Cold Spring Harbor Laboratory (1988). For example, 15-mer peptides having a sequence encoded by the appropriate identified
25 gene sequence of interest or portion thereof can be chemically synthesized. The synthetic peptides are injected into mice to generate antibodies to the polypeptide encoded by the identified nucleic acid sequence of interest or portion thereof. Alternatively, samples of the protein expressed from the expression vectors discussed above can be purified and subjected to amino acid sequencing analysis to confirm the identity of the recombinantly
30 expressed protein and subsequently used to raise antibodies. An Example describing in detail the generation of monoclonal and polyclonal antibodies appears in Example 7.

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The protein encoded by the identified nucleic acid sequence of interest or portion thereof can be purified using standard immunochromatography techniques. In such procedures, a solution containing the secreted protein, such as the culture medium or a cell extract, is applied to a column having antibodies against the secreted protein attached to the chromatography matrix. The secreted protein is allowed to bind the immunochromatography column. Thereafter, the column is washed to remove non-specifically bound proteins. The specifically bound secreted protein is then released from the column and recovered using standard techniques. These procedures are well known in the art.

In an alternative protein purification scheme, the identified nucleic acid sequence of interest or portion thereof can be incorporated into expression vectors designed for use in purification schemes employing chimeric polypeptides. In such strategies the coding sequence of the identified nucleic acid sequence of interest or portion thereof is inserted in-frame with the gene encoding the other half of the chimera. The other half of the chimera can be maltose binding protein (MBP) or a nickel binding polypeptide encoding sequence. A chromatography matrix having antibody to MBP or nickel attached thereto is then used to purify the chimeric protein. Protease cleavage sites can be engineered between the MBP gene or the nickel binding polypeptide and the identified expected gene of interest, or portion thereof. Thus, the two polypeptides of the chimera can be separated from one another by protease digestion.

One useful expression vector for generating maltose binding protein fusion proteins is pMAL (New England Biolabs), which encodes the *malE* gene. In the pMal protein fusion system, the cloned gene is inserted into a pMal vector downstream from the *malE* gene. This results in the expression of an MBP-fusion protein. The fusion protein is purified by affinity chromatography. These techniques as described are well known to those skilled in the art of molecular biology.

EXAMPLE 7

Production of an Antibody to an isolated *E. coli* Protein

Substantially pure protein or polypeptide is isolated from the transformed cells as described in Example 6. The concentration of protein in the final preparation is adjusted, for example, by concentration on a 10,000 molecular weight cut off AMICON filter device

(Millipore, Bedford, MA), to the level of a few micrograms/ml. Monoclonal or polyclonal antibody to the protein can then be prepared as follows:

Monoclonal Antibody Production by Hybridoma Fusion

Monoclonal antibody to epitopes of any of the peptides identified and isolated as described can be prepared from murine hybridomas according to the classical method of Kohler, G. and Milstein, C., **Nature** **256**:495 (1975) or any of the well-known derivative methods thereof. Briefly, a mouse is repetitively inoculated with a few micrograms of the selected protein or peptides derived therefrom over a period of a few weeks. The mouse is then sacrificed, and the antibody producing cells of the spleen isolated. The spleen cells are fused by means of polyethylene glycol with mouse myeloma cells, and the excess unfused cells destroyed by growth of the system on selective media comprising aminopterin (HAT media). The successfully fused cells are diluted and aliquots of the dilution placed in wells of a microtiter plate where growth of the culture is continued. Antibody-producing clones are identified by detection of antibody in the supernatant fluid of the wells by immunoassay procedures, such as ELISA, as described by Engvall, E., "Enzyme immunoassay ELISA and EMIT," **Meth. Enzymol.** **70**:419 (1980), and derivative methods thereof. Selected positive clones can be expanded and their monoclonal antibody product harvested for use. Detailed procedures for monoclonal antibody production are described in Davis, L. et al. **Basic Methods in Molecular Biology** Elsevier, New York. Section 21-2.

Polyclonal Antibody Production by Immunization

Polyclonal antiserum containing antibodies to heterogeneous epitopes of a single protein or a peptide can be prepared by immunizing suitable animals with the expressed protein or peptides derived therefrom described above, which can be unmodified or modified to enhance immunogenicity. Effective polyclonal antibody production is affected by many factors related both to the antigen and the host species. For example, small molecules tend to be less immunogenic than larger molecules and can require the use of carriers and adjuvant. Also, host animals vary in response to site of inoculations and dose, with both inadequate or excessive doses of antigen resulting in low titer antisera. Small doses (ng level) of antigen administered at multiple intradermal sites appears to be most reliable. An effective immunization protocol for rabbits can be found in Vaitukaitis, J. et al. **J. Clin. Endocrinol. Metab.** **33**:988-991 (1971).

Booster injections can be given at regular intervals, and antiserum harvested when antibody titer thereof, as determined semi-quantitatively, for example, by double immunodiffusion in agar against known concentrations of the antigen, begins to fall. See, for example, Ouchterlony, O. et al., Chap. 19 in: **Handbook of Experimental Immunology** D. Wier (ed) Blackwell (1973). Plateau concentration of antibody is usually in the range of 0.1 to 0.2 mg/ml of serum (about 12 μ M). Affinity of the antisera for the antigen is determined by preparing competitive binding curves, as described, for example, by Fisher, D., Chap. 42 in: **Manual of Clinical Immunology**, 2d Ed. (Rose and Friedman, Eds.) Amer. Soc. For Microbiol., Washington, D.C. (1980).

Antibody preparations prepared according to either protocol are useful in quantitative immunoassays which determine concentrations of antigen-bearing substances in biological samples; they are also used semi-quantitatively or qualitatively to identify the presence of antigen in a biological sample. The antibodies can also be used in therapeutic compositions for killing bacterial cells expressing the protein.

EXAMPLE 8

Screening Chemical Libraries

A. Protein-Based Assays

Having isolated and expressed bacterial proteins shown to be required for bacterial proliferation, the present invention further contemplates the use of these expressed proteins in assays to screen libraries of compounds for potential drug candidates. The generation of chemical libraries is well known in the art. For example combinatorial chemistry can be used to generate a library of compounds to be screened in the assays described herein. A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis by combining a number of chemical “building blocks” reagents. For example, a linear combinatorial chemical library such as a polypeptide library is formed by combining amino acids in every possible combination to yield peptides of a given length. Millions of chemical compounds theoretically can be synthesized through such combinatorial mixings of chemical building blocks. For example, one commentator observed that the systematic, combinatorial mixing of 100 interchangeable chemical building blocks results in the theoretical synthesis of 100 million tetrameric compounds or 10 billion pentameric compounds. (Gallop et al., “Applications of Combinatorial Technologies to Drug Discovery, Background and Peptide

Combinatorial Libraries,” **Journal of Medicinal Chemistry**, Vol. 37, No. 9, 1233-1250 (1994). Other chemical libraries known to those in the art may also be used, including natural product libraries.

Once generated, combinatorial libraries can be screened for compounds that possess desirable biological properties. For example, compounds which may be useful as drugs or to develop drugs would likely have the ability to bind to the target protein identified, expressed and purified as discussed above. Further, if the identified target protein is an enzyme, candidate compounds would likely interfere with the enzymatic properties of the target protein. Any enzyme can be a target protein. For example, the enzymatic function of a target protein can be to serve as a protease, nuclease, phosphatase, dehydrogenase, transporter protein, transcriptional enzyme, and any other type of enzyme known or unknown. Thus, the present invention contemplates using the protein products described above to screen combinatorial chemical libraries.

Those in the art will appreciate that a number of techniques exist for characterizing target proteins in order to identify molecules useful for the discovery and development of therapeutics. For example, some techniques involve the generation and use of small peptides to probe and analyze target proteins both biochemically and genetically in order to identify and develop drug leads. Such techniques include the methods described in PCT publications No. WO9935494, WO9819162, WO9954728, the disclosures of which are incorporated herein by reference in their entireties.

In another example, the target protein is a serine protease and the substrate of the enzyme is known. The present example is directed towards the analysis of libraries of compounds to identify compounds that function as inhibitors of the target enzyme. First, a library of small molecules is generated using methods of combinatorial library formation well known in the art. U.S. Patent NOs. 5,463,564 and 5,574, 656, to Agrafiotis, et al., entitled “System and Method of Automatically Generating Chemical Compound with Desired Properties,” are two such teachings. Then the library compounds are screened to identify library compounds that possess desired structural and functional properties. U.S. Patent No. 5,684,711 also discusses a method for screening libraries.

To illustrate the screening process, the combined target and chemical compounds of the library are exposed to and permitted to interact with the purified enzyme. A labeled substrate is added to the incubation. The label on the substrate is such that a detectable

signal is emitted from metabolized substrate molecules. The emission of this signal permits one to measure the effect of the combinatorial library compounds on the enzymatic activity of target enzymes. The characteristics of each library compound is encoded so that compounds demonstrating activity against the enzyme can be analyzed and features common to the various compounds identified can be isolated and combined into future iterations of libraries.

Once a library of compounds is screened, subsequent libraries are generated using those chemical building blocks that possess the features shown in the first round of screen to have activity against the target enzyme. Using this method, subsequent iterations of candidate compounds will possess more and more of those structural and functional features required to inhibit the function of the target enzyme, until a group of enzyme inhibitors with high specificity for the enzyme can be found. These compounds can then be further tested for their safety and efficacy as antibiotics for use in mammals.

It will be readily appreciated that this particular screening methodology is exemplary only. Other methods are well known to those skilled in the art. For example, a wide variety of screening techniques are known for a large number of naturally-occurring targets when the biochemical function of the target protein is known.

B. Cell Based Assays

Current cell-based assays used to identify or to characterize compounds for drug discovery and development frequently depend on detecting the ability of a test compound to inhibit the activity of a target molecule located within a cell or located on the surface of a cell. Most often such target molecules are proteins such as enzymes, receptors and the like. However, target molecules may also include other molecules such as DNAs, lipids, carbohydrates and RNAs including messenger RNAs, ribosomal RNAs, tRNAs and the like. A number of highly sensitive cell-based assay methods are available to those of skill in the art to detect binding and interaction of test compounds with specific target molecules. However, these methods are generally not highly effective when the test compound binds to or otherwise interacts with its target molecule with moderate or low affinity. In addition, the target molecule may not be readily accessible to a test compound in solution, such as when the target molecule is located inside the cell or within a cellular compartment such as the periplasm of a

bacterial cell. Thus, current cell-based assay methods are limited in that they are not effective in identifying or characterizing compounds that interact with their targets with moderate to low affinity or compounds that interact with targets that are not readily accessible.

5 Cell-based assay methods of the present invention have substantial advantages over current cell-based assays practiced in the art. These advantages derive from the use of sensitized cells in which the level or activity of a proliferation-required gene product (the target molecule) has been specifically reduced to the point where the presence or absence of its function becomes a rate-determining step for cellular proliferation. Bacterial, fungal, plant, or animal cells can all be used with the present method. Such sensitized cells become much more sensitive to compounds that are active against the affected target molecule. Thus, cell-based assays of the present invention are capable of detecting compounds exhibiting low or moderate potency against the target molecule of interest because such compounds are substantially more potent on sensitized cells than on non-sensitized cells. The affect may be such that a test compound may be two to several times more potent, at least 10 times more potent or even at least 100 times more potent when tested on the sensitized cells as compared to the non-sensitized cells.

20 Due in part to the increased appearance of antibiotic resistance in pathogenic microorganisms and to the significant side-effects associated with some currently used antibiotics, novel antibiotics acting at new targets are highly sought after in the art. Yet, another limitation in the current art related to cell-based assays is the problem of identifying hits against the same kinds of target molecules in the same limited set of biological pathways over and over again. This may occur when compounds acting at such new targets are discarded, ignored or fail to be detected because compounds acting at the "old" targets are encountered more frequently and are more potent than compounds acting at the new targets. As a result, the majority of antibiotics in use currently interact with a relatively small number of target molecules within an even more limited set of biological pathways.

30 The use of sensitized cells of the current invention provides a solution to the above problem in two ways. First, desired compounds acting at a target of interest, whether a new target or a previously known but poorly exploited target, can now be

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detected above the "noise" of compounds acting at the "old" targets due to the specific and substantial increase in potency of such desired compounds when tested on the sensitized cells of the current invention. Second, the methods used to sensitize cells to compounds acting at a target of interest may also sensitize these cells to compounds acting at other target molecules within the same biological pathway. For example, expression of an antisense molecule to a gene encoding a ribosomal protein is expected to sensitize the cell to compounds acting at that ribosomal protein and may also sensitize the cells to compounds acting at any of the ribosomal components (proteins or rRNA) or even to compounds acting at any target which is part of the protein synthesis pathway. Thus an important advantage of the present invention is the ability to reveal new targets and pathways that were previously not readily accessible to drug discovery methods.

Sensitized cells of the present invention are prepared by reducing the activity or level of a target molecule. The target molecule may be a gene product, such as an RNA or polypeptide produced from the proliferation-required nucleic acids described herein. Alternatively, the target may be a gene product such as an RNA or polypeptide which is produced from a sequence within the same operon as the proliferation-required nucleic acids described herein. In addition, the target may be an RNA or polypeptide in the same biological pathway as the proliferation-required nucleic acids described herein. Such biological pathways include, but are not limited to, enzymatic, biochemical and metabolic pathways as well as pathways involved in the production of cellular structures such as the cell wall.

Current methods employed in the arts of medicinal and combinatorial chemistries are able to make use of structure-activity relationship information derived from testing compounds in various biological assays including direct binding assays and cell-based assays. Occasionally compounds are directly identified in such assays that are sufficiently potent to be developed as drugs. More often, initial hit compounds exhibit moderate or low potency. Once a hit compound is identified with low or moderate potency, directed libraries of compounds are synthesized and tested in order to identify more potent leads. Generally these directed libraries are combinatorial chemical libraries consisting of compounds with structures related to the hit compound but containing systematic variations including additions, subtractions and substitutions

of various structural features. When tested for activity against the target molecule, structural features are identified that either alone or in combination with other features enhance or reduce activity. This information is used to design subsequent directed libraries containing compounds with enhanced activity against the target molecule. After one or several iterations of this process, compounds with substantially increased activity against the target molecule are identified and may be further developed as drugs. This process is facilitated by use of the sensitized cells of the present invention since compounds acting at the selected targets exhibit increased potency in such cell-based assays, thus; more compounds can now be characterized providing more useful information than would be obtained otherwise.

Thus, it is now possible using cell-based assays of the present invention to identify or characterize compounds that previously would not have been readily identified or characterized including compounds that act at targets that previously were not readily exploited using cell-based assays. The process of evolving potent drug leads from initial hit compounds is also substantially improved by the cell-based assays of the present invention because, for the same number of test compounds, more structure-function relationship information is likely to be revealed.

The method of sensitizing a cell entails selecting a suitable gene or operon. A suitable gene or operon is one whose expression is required for the proliferation of the cell to be sensitized. The next step is to introduce into the cells to be sensitized, an antisense RNA capable of hybridizing to the suitable gene or operon or to the RNA encoded by the suitable gene or operon. Introduction of the antisense RNA can be in the form of an expression vector in which antisense RNA is produced under the control of an inducible promoter. The amount of antisense RNA produced is limited by varying the inducer concentration to which the cell is exposed and thereby varying the activity of the promoter driving transcription of the antisense RNA. Thus, cells are sensitized by exposing them to an inducer concentration that results in a sub-lethal level of antisense RNA expression.

In one embodiment of the cell-based assays, the identified exogenous *E. coli* nucleotide sequences of the present invention are used to inhibit the production of a proliferation-required protein. Expression vectors producing antisense RNA against identified genes required for proliferation are used to limit the concentration of a

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proliferation-required protein without severely inhibiting growth. To achieve that goal, a growth inhibition dose curve of inducer is calculated by plotting various doses of inducer against the corresponding growth inhibition caused by the antisense expression. From this curve, various percentages of antisense induced growth inhibition, from 1 to 100% can be determined. If the promoter contained in the expression vector contains a *lac* operator the transcription is regulated by *lac* repressor and expression from the promoter is inducible with IPTG. For example, the highest concentration of the inducer IPTG that does not reduce the growth rate (0% growth inhibition) can be predicted from the curve. Cellular proliferation can be monitored by growth medium turbidity via OD measurements. In another example, the concentration of inducer that reduces growth by 25% can be predicted from the curve. In still another example, a concentration of inducer that reduces growth by 50% can be calculated. Additional parameters such as colony forming units (cfu) can be used to measure cellular viability.

Cells to be assayed are exposed to the above-determined concentrations of inducer. The presence of the inducer at this sub-lethal concentration reduces the amount of the proliferation required gene product to the lowest amount in the cell that will support growth. Cells grown in the presence of this concentration of inducer are therefore specifically more sensitive to inhibitors of the proliferation-required protein or RNA of interest or to inhibitors of proteins or RNAs in the same biological pathway as the proliferation-required protein or RNA of interest but not to inhibitors of unrelated proteins or RNAs.

Cells pretreated with sub-inhibitory concentrations of inducer and thus containing a reduced amount of proliferation-required target gene product are then used to screen for compounds that reduce cell growth. The sub-lethal concentration of inducer may be any concentration consistent with the intended use of the assay to identify candidate compounds to which the cells are more sensitive. For example, the sub-lethal concentration of the inducer may be such that growth inhibition is at least about 5%, at least about 8%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60% at least about 75%, or more. Cells which are pre-sensitized using the preceding method are more sensitive to inhibitors of the target protein because these cells contain less target protein to inhibit than wild-type cells.

In another embodiment of the cell based assays of the present invention, the level or activity of a proliferation required gene product is reduced using a temperature sensitive ...mutation in the proliferation-required sequence and an antisense nucleic acid against the proliferation-required sequence. Growing the cells at an intermediate temperature between the permissive and restrictive temperatures of the temperature sensitive mutant where the mutation is in a proliferation-required gene produces cells with reduced activity of the proliferation-required gene product. The antisense RNA directed against the proliferation-required sequence further reduces the activity of the proliferation required gene product. Drugs that may not have been found using either the temperature sensitive mutation or the antisense nucleic acid alone may be identified by determining whether cells in which expression of the antisense nucleic acid has been induced and which are grown at a temperature between the permissive temperature and the restrictive temperature are substantially more sensitive to a test compound than cells in which expression of the antisense nucleic acid has not been induced and which are grown at a permissive temperature. Also drugs found previously from either the antisense nucleic acid alone or the temperature sensitive mutation alone may have a different sensitivity profile when used in cells combining the two approaches, and that sensitivity profile may indicate a more specific action of the drug in inhibiting one or more activities of the gene product.

Temperature sensitive mutations may be located at different sites within the gene and correspond to different domains of the protein. For example, the *dnaB* gene of *Escherichia coli* encodes the replication fork DNA helicase. DnaB has several domains, including domains for oligomerization, ATP hydrolysis, DNA binding, interaction with primase, interaction with DnaC, and interaction with DnaA [(Biswas, E.E. and Biswas, S.B. 1999. Mechanism and DnaB helicase of *Escherichia coli*: structural domains involved in ATP hydrolysis, DNA binding, and oligomerization. *Biochem.* **38**:10919-10928; Hiasa, H. and Marians, K.J. 1999. Initiation of bidirectional replication at the chromosomal origin is directed by the interaction between helicase and primase. *J. Biol. Chem.* **274**:27244-27248; San Martin, C., Radermacher, M., Wolpensinger, B., Engel, A., Miles, C.S., Dixon, N.E., and Carazo, J.M. 1998. Three-dimensional reconstructions from cryoelectron microscopy images reveal an intimate complex between helicase DnaB and its loading partner DnaC. *Structure* **6**:501-9;

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5 Sutton, M.D., Carr, K.M., Vicente, M., and Kaguni, J.M. 1998. *Escherichia coli* DnaA protein. The N-terminal domain and loading of DnaB helicase at the *E. coli* chromosomal. J. Biol. Chem. **273**:34255-62.), the disclosures of which are incorporated herein by reference in their entireties]. Temperature sensitive mutations in different domains of DnaB confer different phenotypes at the restrictive temperature, which include either an abrupt stop or slow stop in DNA replication with or without DNA breakdown (Wechsler, J.A. and Gross, J.D. 1971. *Escherichia coli* mutants temperature-sensitive for DNA synthesis. Mol. Gen. Genetics **113**:273-284, the disclosure of which is incorporated herein by reference in its entirety) and termination of growth or cell death. Combining the use of temperature sensitive mutations in the *dnaB* gene that cause cell death at the restrictive temperature with an antisense to the *dnaB* gene could lead to the discovery of very specific and effective inhibitors of one or a subset of activities exhibited by DnaB.

15 When screening for antimicrobial agents against a gene product required for proliferation, growth inhibition of cells containing a limiting amount of that proliferation-required gene product can be assayed. Growth inhibition can be measured by directly comparing the amount of growth, measured by the optical density of the growth medium, between an experimental sample and a control sample. Alternative methods for assaying cell proliferation include measuring green fluorescent protein (GFP) reporter construct emissions, various enzymatic activity assays, and other methods well known in the art.

20 It will be appreciated that the above method may be performed in solid phase, liquid phase or a combination of the two. For example, cells grown on nutrient agar containing the inducer of the antisense construct may be exposed to compounds spotted onto the agar surface. A compound's effect may be judged from the diameter of the resulting killing zone, the area around the compound application point in which cells do not grow. Multiple compounds may be transferred to agar plates and simultaneously tested using automated and semi-automated equipment including but not restricted to multi-channel pipettes (for example the Beckman Multimek) and multi-channel spotters (for example the Genomic Solutions Flexys). In this way multiple plates and thousands to millions of compounds may be tested per day.

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The compounds may also be tested entirely in liquid phase using microtiter plates as described below. Liquid phase screening may be performed in microtiter plates containing 96, 384, 1536 or more wells per microtiter plate to screen multiple plates and thousands to millions of compounds per day. Automated and semi-automated equipment may be used for addition of reagents (for example cells and compounds) and determination of cell density.

EXAMPLE 9

The effectiveness of the above cell based assay was validated using constructs expressing antisense RNA to *E. coli* genes *rplL*, *rplJ*, and *rplW* encoding ribosomal proteins L7/L12, L10 and L23 respectively. These proteins are part of the protein synthesis apparatus of the cell and as such are required for proliferation. These constructs were used to test the effect of antisense expression on cell sensitivity to antibiotics known to bind to the ribosome and thereby inhibit protein synthesis. Constructs expressing antisense RNA to several other genes (*elaD*, *visC*, *yohH*, and *aptE/B*), the products of which are not involved in protein synthesis were used for comparison.

First expression vectors containing antisense constructs to either *rplW* or to *elaD* were introduced into separate *E. coli* cell populations. Vector introduction is a technique well known to those of ordinary skill in the art. The expression vectors of this example contain IPTG inducible promoters that drive the expression of the antisense RNA in the presence of the inducer. However, those skilled in the art will appreciate that other inducible promoters may also be used. Suitable expression vectors are also well known in the art. The *E. coli* antisense clones encoding ribosomal proteins L7/L12, L10 and L23 were used to test the effect of antisense expression on cell sensitivity to the antibiotics known to bind to these proteins. First, expression vectors containing antisense to either the genes encoding L7/L12 and L10 or L23 were introduced into separate *E. coli* cell populations.

The cell populations were exposed to a range of IPTG concentrations in liquid medium to obtain the growth inhibitory dose curve for each clone (Fig. 1). First, seed cultures were grown to a particular turbidity that is measured by the optical density (OD) of the growth solution. The OD of the solution is directly related to the number of bacterial cells contained therein. Subsequently, sixteen 200 ul liquid medium cultures

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were grown in a 96 well microtiter plate at 37 C with a range of IPTG concentrations in duplicate two-fold serial dilutions from 1600 uM to 12.5 uM (final concentration). Additionally, control cells were grown in duplicate without IPTG. These cultures were started from equal amounts of cells derived from the same initial seed culture of a clone of interest. The cells were grown for up to 15 hours and the extent of growth was determined by measuring the optical density of the cultures at 600 nm. When the control culture reached mid-log phase the percent growth of the control for each of the IPTG containing cultures was plotted against the log concentrations of IPTG to produce a growth inhibitory dose response curve for the IPTG. The concentration of IPTG that inhibits cell growth to 50% (IC₅₀) as compared to the 0 mM IPTG control (0% growth inhibition) was then calculated from the curve. Under these conditions, an amount of antisense RNA was produced that reduced the expression levels of *rplW* and *elaD* to a degree such that growth was inhibited by 50%.

Alternative methods of measuring growth are also contemplated. Examples of these methods include measurements of proteins, the expression of which is engineered into the cells being tested and can readily be measured. Examples of such proteins include green fluorescent protein (GFP) and various enzymes.

Cells were pretreated with the selected concentration of IPTG and then used to test the sensitivity of cell populations to tetracycline, erythromycin and other protein synthesis inhibitors. An example of a tetracycline dose response curve is shown in Figures 2A and 2B for the *rplW* and *elaD* genes, respectively. Cells were grown to log phase and then diluted into media alone or media containing IPTG at concentrations which give 20% and 50% growth inhibition as determined by IPTG dose response curves. After 2.5 hours, the cells were diluted to a final OD₆₀₀ of 0.002 into 96 well plates containing (1) +/- IPTG at the same concentrations used for the 2.5 hour pre-incubation; and (2) serial two-fold dilutions of tetracycline such that the final concentrations of tetracycline range from 1 µg/ml to 15.6 ng/ml and 0 µg/ml. The 96 well plates were incubated at 37°C and the OD₆₀₀ was read by a plate reader every 5 minutes for up to 15 hours. For each IPTG concentration and the no IPTG control, tetracycline dose response curves were determined when the control (absence of tetracycline) reached 0.1 OD₆₀₀. To compare tetracycline sensitivity with and without IPTG, tetracycline IC₅₀s were determined from the dose response curves (Figs. 2A-B).

Cells with reduced levels of L23 (*rplW*) showed increased sensitivity to tetracycline (Fig. 2A) as compared to cells with reduced levels of *elaD* (Fig. 2B). Figure 3 shows a summary bar chart in which the ratios of tetracycline IC50s determined in the presence of IPTG which gives 50% growth inhibition versus tetracycline IC50s determined without IPTG (fold increase in tetracycline sensitivity) were plotted. Cells with reduced levels of either L7/L12 (genes *rplL*, *rplJ*) or L23 (*rplW*) showed increased sensitivity to tetracycline (Fig. 3). Cells expressing antisense to genes not known to be involved in protein synthesis (*atpB/E*, *visC*, *elaD*, *yohH*) did not show the same increased sensitivity to tetracycline, validating the specificity of this assay (Fig. 3).

In addition to the above, it has been observed in initial experiments that clones expressing antisense RNA to genes involved in protein synthesis (including genes encoding ribosomal proteins L7/L12 & L10, L7/L12 alone, L22, and L18, as well as genes encoding rRNA and Elongation Factor G) have increased sensitivity to the macrolide, erythromycin, whereas clones expressing antisense to the non-protein synthesis genes *elaD*, *atpB/E* and *visC* do not. Furthermore, the clone expressing antisense to *rplL* and *rplJ* does not show increased sensitivity to nalidixic acid and ofloxacin, antibiotics which do not inhibit protein synthesis.

The results with the ribosomal protein genes *rplL*, *rplJ*, and *rplW* as well as the initial results using various other antisense clones and antibiotics show that limiting the concentration of an antibiotic target makes cells more sensitive to the antimicrobial agents that specifically interact with that protein. The results also show that these cells are sensitized to antimicrobial agents that inhibit the overall function in which the protein target is involved but are not sensitized to antimicrobial agents that inhibit other functions.

The cell based assay described above may also be used to identify the biological pathway in which a proliferation-required nucleic acid or its gene product lies. In such methods, cells expressing a sub-lethal level of antisense to a target proliferation-required nucleic acid and control cells in which expression of the antisense has not been induced are contacted with a panel of antibiotics known to act in various pathways. If the antibiotic acts in the pathway in which the target proliferation-required nucleic acid or its gene product lies, cells in which expression of the antisense has been induced will

be more sensitive to the antibiotic than cells in which expression of the antisense has not been induced.

As a control, the results of the assay may be confirmed by contacting a panel of cells expressing antisense nucleic acids to many different proliferation-required genes including the target proliferation-required gene. If the antibiotic is acting specifically, heightened sensitivity to the antibiotic will be observed only in the cells expressing antisense to a target proliferation-required gene (or cells expressing antisense to other proliferation-required genes in the same pathway as the target proliferation-required gene) but will not be observed generally in all cells expressing antisense to proliferation-required genes.

Similarly, the above method may be used to determine the pathway on which a test antibiotic acts. A panel of cells, each of which expresses antisense to a proliferation-required nucleic acid in a known pathway, is contacted with a compound for which it is desired to determine the pathway on which it acts. The sensitivity of the panel of cells to the test compound is determined in cells in which expression of the antisense has been induced and in control cells in which expression of the antisense has not been induced. If the test antibiotic acts on the pathway on which an antisense nucleic acid acts, cells in which expression of the antisense has been induced will be more sensitive to the antibiotic than cells in which expression of the antisense has not been induced. In addition, control cells in which expression of antisense to proliferation-required genes in other pathways has been induced will not exhibit heightened sensitivity to the antibiotic. In this way, the pathway on which the test antibiotic acts may be determined.

The Example below provides one method for performing such assays.

EXAMPLE 10

Identification of the Pathway in which a Proliferation-Required Gene Lies or the Pathway on which an Antibiotic Acts

A. Preparation of Bacterial Stocks for Assay

To provide a consistent source of cells to screen, frozen stocks of host bacteria containing the desired antisense construct are prepared using standard microbiological techniques. For example, a single clone of the organism can be isolated by streaking out a sample of the original stock onto an agar plate containing nutrients for cell growth and

an antibiotic for which the antisense construct contains a gene which confers resistance. After overnight growth an isolated colony is picked from the plate with a sterile needle and transferred to an appropriate liquid growth media containing the antibiotic required for maintenance of the plasmid. The cells are incubated at 30°C to 37°C with vigorous shaking for 4 to 6 hours to yield a culture in exponential growth. Sterile glycerol is added to 15% (volume to volume) and 100µL to 500 µL aliquots are distributed into sterile cryotubes, snap frozen in liquid nitrogen, and stored at -80°C for future assays.

B. Growth of Bacteria for Use in the Assay

A day prior to an assay, a stock vial is removed from the freezer, rapidly thawed (37°C water bath) and a loop of culture is streaked out on an agar plate containing nutrients for cell growth and an antibiotic to which the antisense construct confers resistance. After overnight growth at 37°C, ten randomly chosen, isolated colonies are transferred from the plate (sterile inoculum loop) to a sterile tube containing 5 mL of LB medium containing the antibiotic to which the antisense vector confers resistance. After vigorous mixing to form a homogeneous cell suspension, the optical density of the suspension is measured at 600 nm (OD600) and if necessary an aliquot of the suspension is diluted into a second tube of 5 mL, sterile, LB medium plus antibiotic to achieve an $OD_{600} \leq 0.02$ absorbance units. The culture is then incubated at 37° C for 1-2 hrs with shaking until the OD600 reaches OD 0.2 – 0.3. At this point the cells are ready to be used in the assay.

C. Selection of Media to be Used in Assay

Two fold dilution series of the inducer are generated in culture media containing the appropriate antibiotic for maintenance of the antisense construct. Several media are tested side by side and three to four wells are used to evaluate the effects of the inducer at each concentration in each media. For example, M9 minimal media, LB broth, TBD broth and Muller-Hinton media may be tested with the inducer IPTG at the following concentrations, 50 µM, 100 µM, 200 µM, 400 µM, 600 µM, 800 µM and 1000 µM. Equal volumes of test media-inducer and cells are added to the wells of a 384 well microtiter plate and mixed. The cells are prepared as described above and diluted 1:100 in the appropriate media containing the test antibiotic immediately prior to addition to the microtiter plate wells. For a control, cells are also added to several wells of each media that do not contain inducer, for example 0 µM IPTG. Cell growth is monitored

continuously by incubation at 37°C in a microtiter plate reader monitoring the OD600 of the wells over an 18-hour period. The percent inhibition of growth produced by each concentration of inducer is calculated by comparing the rates of logarithmic growth against that exhibited by cells growing in media without inducer. The medium yielding greatest sensitivity to inducer is selected for use in the assays described below.

D. Measurement of Test Antibiotic Sensitivity in the Absence of Antisense Construct Induction

Two-fold dilution series of antibiotics of known mechanism of action are generated in the culture media selected for further assay development that has been supplemented with the antibiotic used to maintain the construct. A panel of test antibiotics known to act on different pathways is tested side by side with three to four wells being used to evaluate the effect of a test antibiotic on cell growth at each concentration. Equal volumes of test antibiotic and cells are added to the wells of a 384 well microtiter plate and mixed. Cells are prepared as described above using the media selected for assay development supplemented with the antibiotic required to maintain the antisense construct and are diluted 1:100 in identical media immediately prior to addition to the microtiter plate wells. For a control, cells are also added to several wells that contain the solvent used to dissolve the antibiotics but no antibiotic. Cell growth is monitored continuously by incubation at 37°C in a microtiter plate reader monitoring the OD600 of the wells over an 18-hour period. The percent inhibition of growth produced by each concentration of antibiotic is calculated by comparing the rates of logarithmic growth against that exhibited by cells growing in media without antibiotic. A plot of percent inhibition against log[antibiotic concentration] allows extrapolation of an IC₅₀ value for each antibiotic.

E. Measurement of Test Antibiotic Sensitivity in the Presence of Antisense Construct Inducer

The culture media selected for use in the assay is supplemented with inducer at concentrations shown to inhibit cell growth by 50 and 80% as described above and the antibiotic used to maintain the construct. Two fold dilution series of the panel of test antibiotics used above are generated in each of these media. Several antibiotics are tested side by side with three to four wells being used to evaluate the effects of an antibiotic on cell growth at each concentration, in each media. Equal volumes of test

antibiotic and cells are added to the wells of a 384 well microtiter plate and mixed. Cells are prepared as described above using the media selected for use in the assay supplemented with the antibiotic required to maintain the antisense construct. The cells are diluted 1:100 into two 50 mL aliquots of identical media containing concentrations of inducer that have been shown to inhibit cell growth by 50% and 80 % respectively and incubated at 37°C with shaking for 2.5 hours. Immediately prior to addition to the microtiter plate wells, the cultures are adjusted to an appropriate OD₆₀₀ (typically 0.002) by dilution into warm (37°C) sterile media supplemented with identical concentrations of the inducer and antibiotic used to maintain the antisense construct. For a control, cells are also added to several wells that contain solvent used to dissolve test antibiotics but which contain no antibiotic. Cell growth is monitored continuously by incubation at 37°C in a microtiter plate reader monitoring the OD600 of the wells over an 18-hour period. The percent inhibition of growth produced by each concentration of antibiotic is calculated by comparing the rates of logarithmic growth against that exhibited by cells growing in media without antibiotic. A plot of percent inhibition against log[antibiotic concentration] allows extrapolation of an IC₅₀ value for each antibiotic.

F. Determining the Specificity of the Test Antibiotics

A comparison of the IC₅₀s generated by antibiotics of known mechanism of action under antisense induced and non-induced conditions allows the pathway in which a proliferation-required nucleic acid lies to be identified. If cells expressing an antisense nucleic acid against a proliferation-required gene are selectively sensitive to an antibiotic acting via a particular pathway, then the gene against which the antisense acts is involved in the pathway in which the antibiotic acts.

G. Identification of Pathway in which a Test Antibiotic Acts

As discussed above, the cell based assay may also be used to determine the pathway against which a test antibiotic acts. In such an analysis, the pathways against which each member of a panel of antisense nucleic acids acts are identified as described above. A panel of cells, each containing an inducible antisense vector against a gene in a known proliferation-required pathway, is contacted with a test antibiotic for which it is desired to determine the pathway on which it acts under inducing an non-inducing conditions. If heightened sensitivity is observed in induced cells expressing antisense against a gene in a particular pathway but not in induced cells expressing antisense

against genes in other pathways, then the test antibiotic acts against the pathway for which heightened sensitivity was observed.

One skilled in the art will appreciate that further optimization of the assay conditions, such as the concentration of inducer used to induce antisense expression and/or the growth conditions used for the assay (for example incubation temperature and media components) may further increase the selectivity and/or magnitude of the antibiotic sensitization exhibited.

The following example confirms the effectiveness of the methods described above.

EXAMPLE 11

Identification of the Pathway in which a Proliferation-Required Gene Lies

Antibiotics of various chemical classes and modes of action were purchased from Sigma Chemicals (St. Louis, MO). Stock solutions were prepared by dissolving each antibiotic in an appropriate aqueous solution based on information provided by the manufacturer. The final working solution of each antibiotic contained no more than 0.2% (w/v) of any organic solvent. To determine their potency against a bacterial strain engineered for expression of an antisense against a proliferation-required 50S ribosomal protein, each antibiotic was serially diluted two or three fold in growth medium supplemented with the appropriate antibiotic for maintenance of the anti-sense construct. At least ten dilutions were prepared for each antibiotic. 25 μ L aliquots of each dilution were transferred to discrete wells of a 384-well microplate (the assay plate) using a multi-channel pipette. Quadruplicate wells were used for each dilution of an antibiotic under each treatment condition (plus and minus inducer). Each assay plate contained twenty wells for cell growth controls (growth media replacing antibiotic), ten wells for each treatment (plus and minus inducer, in this example IPTG). Assay plates were usually divided into the two treatments: half the plate containing induced cells and an appropriate concentrations of inducer (in this example IPTG) to maintain the state of induction, the other half containing non-induced cells in the absence of IPTG.

Cells for the assay were prepared as follows. Bacterial cells containing a construct, from which expression of antisense nucleic acid against rplL and rplJ, which encode proliferation-required 50S ribosomal subunit proteins, is inducible in the presence of IPTG, were grown into exponential growth (OD_{600} 0.2 to 0.3) and then

TABLE IV
Effect of Expression of Antisense RNA to rplL and rplJ on Antibiotic Sensitivity

ANTIBIOTIC CLASS /Names	TARGET	IC50 (-IPTG)	IC50 (+IPTG)	Conc. Unit	Fold Increase in Sensitivity	Sensitivity Increased?
PROTEIN SYNTHESIS INHIBITOR						
ANTIBIOTICS						
AMINOGLYCOSIDES						
Gentamicin	30S ribosome function	2715	19.19	ng/ml	141	Yes
Streptomycin	30S ribosome function	11280	161	ng/ml	70	Yes
Spectinomycin	30S ribosome function	18050	<156	ng/ml		Yes
Tobramycin	30S ribosome function	3594	70.58	ng/ml	51	Yes
MACROLIDES						
Erythromycin	50S ribosome function	7467	187	ng/ml	40	Yes
AROMATIC POLYKETIDES						
Tetracycline	30S ribosome function	199.7	1.83	ng/ml	109	Yes
Minocycline	30S ribosome function	668.4	3.897	ng/ml	172	Yes
Doxycycline	30S ribosome function	413.1	27.81	ng/ml	15	Yes
OTHER PROTEIN SYNTHESIS INHIBITORS						
Fusidic acid	Elongation Factor G function	59990	641	ng/ml	94	Yes
Chloramphenicol	30S ribosome function	465.4	1.516	ng/ml	307	Yes
Lincomycin	50S ribosome function	47150	324.2	ng/ml	145	Yes
OTHER ANTIBIOTIC MECHANISMS						
B-LACTAMS						
Cefoxitin	Cell wall biosynthesis	2782	2484	ng/ml	1	No
Cefotaxime	Cell wall biosynthesis	24.3	24.16	ng/ml	1	No
DNA SYNTHESIS INHIBITORS						
Nalidixic acid	DNA Gyrase activity	6973	6025	ng/ml	1	No
Ofloxacin	DNA Gyrase activity	49.61	45.89	ng/ml	1	No

Cell Sensitivity

OTHER							
Bacitracin	Cell membrane function	4077	4677	mg/ml	1	No	
Trimethoprim	Dihydrofolate Reductase activity	128.9	181.97	ng/ml	1	No	
Vancomycin	Cell wall biosynthesis	145400	72550	ng/ml	2	No	

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The above results demonstrate that induction of an antisense RNA to genes encoding 50S ribosomal subunit proteins results in a selective and highly significant sensitization of cells to antibiotics that inhibit ribosomal function and protein synthesis. The above results further demonstrate that induction of an antisense construct to an essential gene sensitizes an organism to compounds that interfere with that gene products' biological role. This sensitization is restricted to compounds that interfere with pathways associated with the targeted gene and it's product.

Assays utilizing antisense constructs to essential genes can be used to identify compounds that specifically interfere with the activity of multiple targets in a pathway. Such constructs can be used to simultaneously screen a sample against multiple targets in one pathway in one reaction (Combinatorial HTS).

Furthermore, as discussed above, panels of antisense construct containing cells may be used to characterize the point of intervention of any compound affecting an essential biological pathway including antibiotics with no known mechanism of action.

Another embodiment of the present invention is a method for determining the pathway against which a test antibiotic compound is active in which the activity of target proteins or nucleic acids involved in proliferation-required pathways is reduced by contacting cells with a sublethal concentration of a known antibiotic which acts against the target protein or nucleic acid. In one embodiment, the target protein or nucleic acid is a target protein or nucleic acid corresponding to a proliferation-required nucleic acid identified using the methods described above. The method is similar to those described above for determining which pathway a test antibiotic acts against except that rather than reducing the activity or level of a proliferation-required gene product using a sublethal level of antisense to a proliferation-required nucleic acid, the activity or level of the proliferation-required gene product is reduced using sublethal level of a known antibiotic which acts against the proliferation required gene product.

Interactions between drugs which affect the same biological pathway has been described in the literature. For example, Mecillinam (Amdinocillin) binds to and inactivates the penicillin binding protein 2 (PBP2, product of the *mrda* in *E. coli*). This antibiotic inteacts with other antibiotics that inhibit PBP2 as well as antibiotics that inhibit other penicillin binding proteins such as PBP3 [(Gutmann, L., Vincent, S., Billot-Klein, D., Acar, J.F., Mrena, E., and Williamson, R. (1986) Involvement of

penicillin-binding protein 2 with other penicillin-binding proteins in lysis of *Escherichia coli* by some beta-lactam antibiotics alone and in synergistic lytic effect of amdinocillin (mecillinam). Antimicrobial Agents & Chemotherapy, 30:906-912), the disclosure of which is incorporated herein by reference in its entirety]. Interactions

5 between drugs could, therefore, involve two drugs that inhibit the same target protein or nucleic acid or inhibit different proteins or nucleic acids in the same pathway [(Fukuoka, T., Domon, H., Kakuta, M., Ishii, C., Hirasawa, A., Utsui, Y., Ohya, S., and Yasuda, H. (1997) Combination effect between panipenem and vancomycin on highly methicillin-resistant *Staphylococcus aureus*. Japan. J. Antibio. 50:411-419; Smith, C.E.,

10 Foleno, B.E., Barrett, J.F., and Frosc, M.B. (1997) Assessment of the synergistic interactions of levofloxacin and ampicillin against *Enterococcus faecium* by the checkerboard agar dilution and time-kill methods. Diagnos. Microbiol. Infect. Disease 27:85-92; den Hollander, J.G., Horrevorts, A.M., van Goor, M.L., Verbrugh, H.A., and Mouton, J.W. (1997) Synergism between tobramycin and ceftazidime against a resistant

15 *Pseudomonas aeruginosa* strain, tested in an in vitro pharmacokinetic model. Antimicrobial Agents & Chemotherapy. 41:95-110), the disclosure of all of which are incorporated herein by reference in their entireties].

Two drugs may interact even though they inhibit different targets. For example, the proton pump inhibitor, Omeprazole, and the antibiotic, Amoxycillin, two synergistic

20 compounds acting together, can cure *Helicobacter pylori* infection [(Gabryelewicz, A., Laszewicz, W., Dzieniszewski, J., Ciok, J., Marlicz, K., Bielecki, D., Popiela, T., Legutko, J., Knapik, Z., Poniewierka, E. (1997) Multicenter evaluation of dual-therapy (omeprazol and amoxycillin) for *Helicobacter pylori*-associated duodenal and gastric ulcer (two years of the observation). J. Physiol. Pharmacol. 48 Suppl 4:93-105), the

25 disclosure of which is incorporated herein by reference in its entirety].

The growth inhibition from the sublethal concentration of the known antibiotic may be at least about 5%, at least about 8%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, or at least about 75%, or more.

30 Alternatively, the sublethal concentration of the known antibiotic may be determined by measuring the activity of the target proliferation-required gene product rather than by measuring growth inhibition.

Cells are contacted with a combination of each member of a panel of known antibiotics at a sublethal level and varying concentrations of the test antibiotic. As a control, the cells are contacted with varying concentrations of the test antibiotic alone. The IC₅₀ of the test antibiotic in the presence and absence of the known antibiotic is determined. If the IC₅₀s in the presence and absence of the known drug are substantially similar, then the test drug and the known drug act on different pathways. If the IC₅₀s are substantially different, then the test drug and the known drug act on the same pathway.

Another embodiment of the present invention is a method for identifying a candidate compound for use as an antibiotic in which the activity of target proteins or nucleic acids involved in proliferation-required pathways is reduced by contacting cells with a sublethal concentration of a known antibiotic which acts against the target protein or nucleic acid. In one embodiment, the target protein or nucleic acid is a target protein or nucleic acid corresponding to a proliferation-required nucleic acid identified using the methods described above. The method is similar to those described above for identifying candidate compounds for use as antibiotics except that rather than reducing the activity or level of a proliferation-required gene product using a sublethal level of antisense to a proliferation-required nucleic acid, the activity or level of the proliferation-required gene product is reduced using a sublethal level of a known antibiotic which acts against the proliferation required gene product.

The growth inhibition from the sublethal concentration of the known antibiotic may be at least about 5%, at least about 8%, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, or at least about 75%, or more.

Alternatively, the sublethal concentration of the known antibiotic may be determined by measuring the activity of the target proliferation-required gene product rather than by measuring growth inhibition.

In order to characterize test compounds of interest, cells are contacted with a panel of known antibiotics at a sublethal level and one or more concentrations of the test compound. As a control, the cells are contacted with the same concentrations of the test compound alone. The IC₅₀ of the test compound in the presence and absence of the known antibiotic is determined. If the IC₅₀ of the test compound is substantially

different in the presence and absence of the known drug then the test compound is a good candidate for use as an antibiotic. As discussed above, once a candidate compound is identified using the above methods its structure may be optimized using standard techniques such as combinatorial chemistry.

- 5 Representative known antibiotics which may be used in each of the above methods are provided in the table below. However, it will be appreciated that other antibiotics may also be used.

ANTIBIOTIC	INHIBITS/TARGET	RESISTANT MUTANTS
Inhibitors of Transcription		
Rifamycin, 1959 Rifampicin	Inhibits initiation of transcription/ β -subunit RNA polymerase, <i>rpoB</i>	<i>rpoB</i> , <i>crp</i> , <i>cyoA</i>
Rifabutin Rifaximin	Accelerates transcription chain termination/ β -subunit RNA polymerase	<i>rpoB</i>
Streptolydigin	an acyclic ansamycin, inhibits RNA polymerase	<i>rpoB</i>
Streptovaricin	Intercalates between 2 successive G-C pairs, <i>rpoB</i> , inhibits RNA synthesis	<i>pldA</i>
Actinomycin D+EDTA		
Inhibitors of Nucleic Acid Metabolism		
Quinolones, 1962 Nalidixic acid Oxolinic acid	α subunit gyrase and/or topoisomerase IV, <i>gyrA</i>	<i>gyrA</i> or <i>B</i> , <i>icd</i> , <i>sloB</i>
Fluoroquinolones	α subunit gyrase, <i>gyrA</i> and/or topoisomerase IV (probable target in Staph)	<i>gyrA</i>
Ciprofloxacin, 1983		<i>norA</i> (efflux in Staph)
Norfloxacin		<i>hipQ</i>
Coumerins Novobiocin	Inhibits ATPase activity of β -subunit gyrase, <i>gyrB</i>	<i>gyrB</i> , <i>cysB</i> , <i>cysE</i> , <i>nov</i> , <i>ompA</i>
Coumermycin	Inhibits ATPase activity of β -subunit gyrase, <i>gyrB</i>	<i>gyrB</i> , <i>hisW</i>
Albicidin	DNA synthesis	<i>tsx</i> (nucleoside channel)
Metronidazole	Causes single-strand breaks in DNA	<i>nar</i>
Inhibitors of Metabolic Pathways		
Sulfonamides, 1932	blocks synthesis of dihydrofolate, dihydro- pterate synthesis, <i>folP</i>	<i>folP</i> , <i>gpt</i> , <i>pabA</i> , <i>pabB</i> , <i>pabC</i>
Sulfanilamide	Inhibits dihydrofolate reductase, <i>folA</i>	<i>folA</i> , <i>thyA</i>
Trimethoprim, 1962	Nucleoside analogue capable of alkylating sulfhydryl groups, inhibitor of thymidylate synthetase	<i>nupC</i> , <i>pnp</i>
Showdomycin		
Thiolactomycin	type II fatty acid synthase inhibitor	<i>emrB</i>
		<i>fadB</i> , <i>emrB</i> due to gene dosage
Psicofuranine	Adenosine glycoside antibiotic, target is GMP synthetase	<i>guaA</i> , <i>B</i>
Triclosan	Inhibits fatty acid synthesis	<i>fabI</i> (<i>envM</i>)
Diazaborines Isoniazid, Ethionamide	heterocyclic, contains boron, inhibit fatty acid synthesis, enoyl-ACP reductase, <i>fabI</i>	<i>fabI</i> (<i>envM</i>)

Inhibitors of Translation		
Phenylpropanoids		
Chloramphenicol, 1947	Binds to ribosomal peptidyl transfer center preventing peptide translocation/ binds to S6, L3, L6, L14, L16, L25, L26, L27, but preferentially to L16	<i>rrn, cmlA, marA, ompF, ompR</i>
Tetracyclines, 1948, type II polyketides	Binding to 30S ribosomal subunit, "A" site on 30S subunit, blocks peptide elongation, strongest binding to S7	<i>clmA (cmr), mar, ompF</i>
Minocycline		
Doxycycline		
Macrolides (type I polyketides)		
Erythromycin, 1950	Binding to 50 S ribosomal subunit, 23S rRNA, blocks peptide translocation, L15, L4, L12	<i>rrn, rplC, rplD, rplV, mac</i>
Carbomycin, Spiramycin		
etc		
Aminoglycosides Streptomycin, 1944	Irreversible binding to 30S ribosomal subunit, prevents translation or causes mistranslation of mRNA/16S rRNA	<i>rpsL, strC,M, ubiF</i>
Neomycin		<i>atpA-E, ecfB, hemAC,D,E,G, topA, rpsC,D,E, rrn, spcB</i>
Spectinomycin		<i>atpA-atpE, cpxA, ecfB, hemA,B,L, topA</i>
Kanamycin		<i>ksgA,B,C,D, rplB,K, rpsI,N,M,R</i>
Kasugamycin		<i>rplF, ubiF</i>
Gentamicin, 1963		<i>cpxA</i>
Amikacin		<i>rpsL</i>
Paromycin		
Lincosamides		
Lincomycin, 1955	Binding to 50 S ribosomal subunit, blocks peptide translocation	<i>linB, rplN,O, rpsG</i>
Clindamycin		
Streptogramins Virginiamycin, 1955	2 components, Streptogramins A&B, bind to the 50S ribosomal subunit blocking peptide translocation and peptide bond formation	
Pristinamycin		
Synercid: quinupristin /dalfopristin		
Fusidanes	Inhibition of elongation factor G (EF-G) prevents peptide translocation	<i>fusA</i>
Fusidic Acid		
Kirromycin (Mocimycin)	Inhibition of elongation factor TU (EF-Tu), prevents peptide bond formation	<i>tufA,B</i>
Pulvomycin	Binds to and inhibits EF-TU	
Thiopeptin	Sulfur-containing antibiotic, inhibits protein synthesis, EF-G	<i>rplE</i>
Tiamulin	Inhibits protein synthesis	<i>rplC, rplD</i>
Negamycin	Inhibits termination process of protein synthesis	<i>prfB</i>
Oxazolidinones Linezolid	23S rRNA	
Isoniazid		
Nitrofurantoin	Inhibits protein synthesis, nitroreductases convert nitrofurantoin to highly reactive electrophilic intermediates which attack bacterial ribosomal proteins non-specifically	<i>pdx nfnA,B</i>
Pseudomonic Acids Mupirocin (Bactroban)	Inhibition of isoleucyl tRNA synthetase-used for Staph, topical cream, nasal spray	<i>ileS</i>

Indolmycin Viomycin	Inhibits tryptophanyl-tRNA synthetase	<i>trpS</i> <i>rrmA</i> (23S rRNA methyltransferase; mutant has slow growth rate, slow chain elongation rate, and viomycin resistance)
Thiopeptides Thiostrepton Micrococcin	Binds to L11-23S RNA complex Inhibits GTP hydrolysis by EF-G Stimulates GTP hydrolysis by EF-G	

Inhibitors of Cell Walls/Membranes

β-lactams Penicillin, 1929 Ampicillin Methicillin, 1960	Inhibition of one or more cell wall transpeptidases, endopeptidases, and glycosidases (PBPs), of the 12 PBPs only 2 are essential: <i>mrdA</i> (PBP2) and <i>ftsI</i> (<i>pbpB</i> , PBP3)	<i>ampC</i> , <i>ampD</i> , <i>ampE</i> , <i>envZ</i> , <i>galU</i> , <i>hipA</i> , <i>hipQ</i> , <i>ompC</i> , <i>ompF</i> , <i>ompR</i> , <i>ptsI</i> , <i>rfa</i> , <i>tolD</i> , <i>tolE</i>
Cephalosporins, 1962 Mecillinam (amdinocillin)	Binds to and inactivates PBP2 (<i>mrdA</i>) Inactivates PBP3 (<i>ftsI</i>)	<i>tonB</i> <i>alaS</i> , <i>argS</i> , <i>crp</i> , <i>cyaA</i> , <i>envB</i> , <i>mrdA</i> , <i>B</i> , <i>mreB</i> , <i>C</i> , <i>D</i>
Aztreonam (Furazlocillin) Bacilysin, Tetaïne Glycopeptides Vancomycin, 1955	Dipeptide, inhib glucosamine synthase Inhib G+ cell wall syn, binds to terminal D-ala-D-ala of pentapeptide, Prevents dephosphorylation and regeneration of lipid carrier	<i>dppA</i>
Polypeptides Bacitracin	Disrupts multiple aspects of membrane function, including peptidoglycan synthesis, lipoteichoic acid synthesis, and the bacterial membrane potential	<i>rfa</i>
Cyclic lipopeptide Daptomycin, 1980	Surfactant action disrupts cell membrane lipids, binds lipid A moiety of LPS	<i>pmrA</i>
Cyclic polypeptides Polymixin, 1939 Fosfomycin, 1969	Analogue of P-enolpyruvate, inhibits 1 st step in peptidoglycan synthesis - UDP-N-acetylglucosamine enolpyruvyl transferase, <i>murA</i> . Also acts as Immunosuppressant	<i>murA</i> , <i>crp</i> , <i>cyaA</i> <i>glpT</i> , <i>hipA</i> , <i>ptsI</i> , <i>uhpT</i>
Cycloserine	Prevents formation of D-ala dimer, inhibits D-ala ligase, <i>ddlA</i> , <i>B</i>	<i>hipA</i> , <i>cycA</i>
Alafosfalin	phosphonodipeptide, cell wall synthesis inhibitor, potentiator of β-lactams	<i>pepA</i> , <i>tpp</i>

Inhibitors of Protein Processing/Transport

Globomycin	Inhibits signal peptidase II (cleaves prolipoproteins subsequent to lipid modification, <i>lspA</i>)	<i>lpp</i> , <i>dnaE</i>
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EXAMPLE 12

Transfer of Exogenous Nucleic Acid Sequences to other Bacterial Species Using the *E. coli* Expression Vectors or Expression Vectors Functional in Bacterial Species other than *E. coli*.

5 The above methods were validated using antisense nucleic acids which inhibit the growth of *E. coli* which were identified using methods similar to those described above. Expression vectors which inhibited growth of *E. coli* upon induction of antisense RNA expression with IPTG were transformed directly into *Enterobacter cloacae*, *Klebsiella pneumonia* or *Salmonella typhimurium*. The transformed cells were
10 then assayed for growth inhibition according to the method of Example 1. After growth in liquid culture, cells were plated at various serial dilutions and a score determined by calculating the log difference in growth for INDUCED vs. UNINDUCED antisense RNA expression as determined by the maximum 10 fold dilution at which a colony was observed. The results of these experiments are listed below in Table VI. If there was
15 no effect of antisense RNA expression in an organism, the clone is minus in Table VI. In contrast, a positive in Table VI means that at least 10 fold more cells were required to observe a colony on the induced plate than on the non-induced plate under the conditions used and in that organism.

 Sixteen of the construts were found to inhibit growth in all the organisms tested upon induction of antisense RNA expression with IPTG. Those skilled in the art will
20 appreciate that a negative result in a heterologous organism does not mean that that organism is missing that gene nor does it mean that the gene is unessential. However, a positive result means that the heterologous organism contains a homologous gene which is required for proliferation of that organism. The homologous gene may be obtained
25 using the methods described herein. Those cells that are inhibited by antisense may be used in cell based assays as described herein for the identification and characterization of compounds in order to develop antibiotics effective in these organisms. Those skilled in the art will appreciate that an antisense molecule which works in the organism from which it was obtained will not always work in a heterologous organism.

TABLE VI
Sensitivity of Other Microorganisms to Antisense Nucleic Acids That Inhibit
Proliferation in *E. coli*

5

Mol. No.	<i>S. typhimurium</i>	<i>E. cloacae</i>	<i>K. pneumoniae</i>
EcXA001	+	+	-
EcXA004	-	-	-
EcXA005	+	+	+
EcXA006	-	-	-
EcXA007	-	+	-
EcXA008	+	-	+
EcXA010	+	+	+
EcXA011	-	+	-
EcXA012	-	+	-
EcXA013	+	+	+
EcXA014	+	+	-
EcXA015	-	+	+
EcXA016	+	+	+
EcXA017	+	+	+
EcXA018	+	+	+
EcXA019	+	+	+
EcXA020	+	+	+
EcXA021	+	+	+
EcXA023	+	+	+
EcXA024	+	-	+
EcXA025	-	-	-

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Mol. No.	<i>S. typhimurium</i>	<i>E. cloacae</i>	<i>K. pneumoniae</i>
EcXA026	+	+	-
EcXA027	+	+	+
EcXA028	+	-	-
EcXA029	-	-	-
EcXA030	+	+	+
EcXA031	+	-	-
EcXA032	+	-	-
EcXA033	+	+	+
EcXA034	+	+	+
EcXA035	-	-	-
EcXA036	+	-	+
EcXA037	-	+	-
EcXA038	+	+	-
EcXA039	+	-	-
EcXA041	+	+	+
EcXA042	-	+	+
EcXA044	-	-	-
EcXA045	-	+	-
EcXA046	-	-	-
EcXA047	+	+	-
EcXA048	-	-	-
EcXA049	+	-	-
EcXA050	-	-	-

Mol. No.	<i>S. typhimurium</i>	<i>E. cloacae</i>	<i>K. pneumoniae</i>
EcXA051	+	-	-
EcXA052	+	-	-
EcXA053	+	+	+
EcXA054	-	-	+
EcXA055	+	-	-

EXAMPLE 13

Use of Identified Exogenous Nucleic Acid Sequences as Probes

The identified sequence of the present invention can be used as probes to obtain the sequence of additional genes of interest from a second organism. For example, probes to potential bacterial target proteins may be hybridized to nucleic acids from other organisms including other bacteria and higher organisms, to identify homologous sequences. Such hybridization might indicate that the protein encoded by the gene to which the probe corresponds is found in humans and therefore not necessarily a good drug target. Alternatively, the gene can be conserved only in bacteria and therefore would be a good drug target for a broad spectrum antibiotic or antimicrobial.

Probes derived from the identified nucleic acid sequences of interest or portions thereof can be labeled with detectable labels familiar to those skilled in the art, including radioisotopes and non-radioactive labels, to provide a detectable probe. The detectable probe can be single stranded or double stranded and can be made using techniques known in the art, including *in vitro* transcription, nick translation, or kinase reactions. A nucleic acid sample containing a sequence capable of hybridizing to the labeled probe is contacted with the labeled probe. If the nucleic acid in the sample is double stranded, it can be denatured prior to contacting the probe. In some applications, the nucleic acid sample can be immobilized on a surface such as a nitrocellulose or nylon membrane. The nucleic acid sample can comprise nucleic acids obtained from a variety of sources, including genomic DNA, cDNA libraries, RNA, or tissue samples.

Procedures used to detect the presence of nucleic acids capable of hybridizing to the detectable probe include well known techniques such as Southern blotting, Northern blotting, dot blotting, colony hybridization, and plaque hybridization. In some applications, the nucleic acid capable of hybridizing to the labeled probe can be cloned into vectors such as expression vectors, sequencing vectors, or in vitro transcription vectors to facilitate the characterization and expression of the hybridizing nucleic acids in the sample. For example, such techniques can be used to isolate, purify and clone sequences from a genomic library, made from a variety of bacterial species, which are capable of hybridizing to probes made from the sequences identified in Examples 5 and 6.

EXAMPLE 14

Preparation of PCR Primers and Amplification of DNA

The identified *E. coli* genes corresponding directly to or located within the operon of nucleic acid sequences required for proliferation or portions thereof can be used to prepare PCR primers for a variety of applications, including the identification or isolation of homologous sequences from other species, for example *S. typhimurium*, *E. cloacae*, and *Klebsiella pneumoniae*, which contain part or all of the homologous genes. Because homologous genes are related but not identical in sequence, those skilled in the art will often employ degenerate sequence PCR primers. Such degenerate sequence primers are designed based on conserved sequence regions, either known or suspected, such as conserved coding regions. The successful production of a PCR product using degenerate probes generated from the sequences identified herein would indicate the presence of a homologous gene sequence in the species being screened. The PCR primers are at least 10 bases, and preferably at least 20 bases in length. More preferably, the PCR primers are at least 20-30 bases in length. In some embodiments, the PCR primers can be more than 30 bases in length. It is preferred that the primer pairs have approximately the same G/C ratio, so that melting temperatures are approximately the same. A variety of PCR techniques are familiar to those skilled in the art. For a review of PCR technology, see Molecular Cloning to Genetic Engineering White, B.A. Ed. in **Methods in Molecular Biology** 67: Humana Press, Totowa 1997. When the entire coding sequence of the target gene is known, the 5' and 3' regions of the target gene can be used as the sequence source for PCR probe generation. In each of these PCR procedures, PCR primers on either side of the nucleic acid sequences to be amplified are added to a suitably prepared nucleic acid

sample along with dNTPs and a thermostable polymerase such as Taq polymerase, Pfu polymerase, or Vent polymerase. The nucleic acid in the sample is denatured and the PCR primers are specifically hybridized to complementary nucleic acid sequences in the sample. The hybridized primers are extended. Thereafter, another cycle of denaturation, hybridization, and extension is initiated. The cycles are repeated multiple times to produce an amplified fragment containing the nucleic acid sequence between the primer sites.

EXAMPLE 15

Inverse PCR

The technique of inverse polymerase chain reaction can be used to extend the known nucleic acid sequence identified in Examples 5 and 6. The inverse PCR reaction is described generally by Ochman et al., in Ch. 10 of **PCR Technology: Principles and Applications for DNA Amplification**, (Henry A. Erlich, Ed.) W.H. Freeman and Co. (1992). Traditional PCR requires two primers that are used to prime the synthesis of complementary strands of DNA. In inverse PCR, only a core sequence need be known.

Using the sequences identified as relevant from the techniques taught in Examples 5 and 6 and applied to other species of bacteria, a subset of exogenous nucleic sequences are identified that correspond to genes or operons that are required for bacterial proliferation. In species for which a genome sequence is not known, the technique of inverse PCR provides a method for obtaining the gene in order to determine the sequence or to place the probe sequences in full context to the target sequence to which the identified exogenous nucleic acid sequence binds.

To practice this technique, the genome of the target organism is digested with an appropriate restriction enzyme so as to create fragments of nucleic acid that contain the identified sequence as well as unknown sequences that flank the identified sequence. These fragments are then circularized and become the template for the PCR reaction. PCR primers are designed in accordance with the teachings of Example 15 and directed to the ends of the identified sequence are synthesized. The primers direct nucleic acid synthesis away from the known sequence and toward the unknown sequence contained within the circularized template. After the PCR reaction is complete, the resulting PCR products can be sequenced so as to extend the sequence of the identified gene past the core sequence of the identified exogenous nucleic acid sequence identified. In this manner, the full

sequence of each novel gene can be identified. Additionally the sequences of adjacent coding and noncoding regions can be identified.

EXAMPLE 16

Identification of Genes Required for *Staphylococcus aureus* Proliferation

Genes required for proliferation in *Staphylococcus aureus* are identified according to the methods described above.

EXAMPLE 17

Identification of Genes Required for *Neisseria gonorrhoeae* Proliferation

Genes required for proliferation in *Neisseria gonorrhoeae* are identified according to the methods described above.

EXAMPLE 18

Identification of Genes Required for *Pseudomonas aeruginosa* Proliferation

Genes required for proliferation in *Pseudomonas aeruginosa* are identified according to the methods described above.

EXAMPLE 19

Identification of Genes Required for *Enterococcus faecalis* Proliferation

Genes required for proliferation in *Enterococcus faecalis* are identified according to the methods described above.

EXAMPLE 20

Identification of Genes Required for *Haemophilus influenzae* Proliferation

Genes required for proliferation in *Haemophilus influenzae* are identified according to the methods described above.

EXAMPLE 21

Identification of Genes Required for *Salmonella typhimurium* Proliferation

Genes required for proliferation in *Salmonella typhimurium* are identified according to the methods described above.

EXAMPLE 22

Identification of Genes Required for *Helicobacter pylori* Proliferation

Genes required for proliferation in *Helicobacter pylori* are identified according to the methods described above.

EXAMPLE 23

Identification of Genes Required for *Mycoplasma pneumoniae* Proliferation

Genes required for proliferation in *Mycoplasma pneumoniae* are identified according to the methods described above.

EXAMPLE 24

Identification of Genes Required for *Plasmodium ovale* Proliferation

5 Genes required for proliferation in *Plasmodium ovale* are identified according to the methods described above.

EXAMPLE 25

Identification of Genes Required for *Saccharomyces cerevisiae* Proliferation

10 Genes required for proliferation in *Saccharomyces cerevisiae* are identified according to the methods described above.

EXAMPLE 26

Identification of Genes Required for *Entamoeba histolytica* Proliferation

Genes required for proliferation in *Entamoeba histolytica* are identified according to the methods described above.

15 EXAMPLE 27

Identification of Genes Required for *Candida albicans* Proliferation

Genes required for proliferation in *Candida albicans* are identified according to the methods described above.

EXAMPLE 28

20 Identification of Genes Required for *Klebsiella pneumoniae* Proliferation

Genes required for proliferation in *Klebsiella pneumoniae* are identified according to the methods described above.

EXAMPLE 29

Identification of Genes Required for *Salmonella typhi* Proliferation

25 Genes required for proliferation in *Salmonella typhi* are identified according to the methods described above.

EXAMPLE 30

Identification of Genes Required for *Salmonella paratyphi* Proliferation

30 Genes required for proliferation in *Salmonella paratyphi* are identified according to the methods described above.

EXAMPLE 31

Identification of Genes Required for *Salmonella choleraesuis* Proliferation

Genes required for proliferation in *Salmonella choleraesuis* are identified according to the methods described above.

EXAMPLE 32

Identification of Genes Required for *Staphylococcus epidermis* Proliferation

5 Genes required for proliferation in *Staphylococcus epidermis* are identified according to the methods described above.

EXAMPLE 33

Identification of Genes Required for *Mycobacterium tuberculosis* Proliferation

10 Genes required for proliferation in *Mycobacterium tuberculosis* are identified according to the methods described above.

EXAMPLE 34

Identification of Genes Required for *Mycobacterium leprae* Proliferation

Genes required for proliferation in *Mycobacterium leprae* are identified according to the methods described above.

EXAMPLE 35

Identification of Genes Required for *Treponema pallidum* Proliferation

Genes required for proliferation in *Treponema pallidum* are identified according to the methods described above.

EXAMPLE 36

Identification of Genes Required for *Bacillus anthracis* Proliferation

Genes required for proliferation in *Bacillus anthracis* are identified according to the methods described above.

EXAMPLE 37

Identification of Genes Required for *Yersinia pestis* Proliferation

25 Genes required for proliferation in *Yersinia pestis* are identified according to the methods described above.

EXAMPLE 38

Identification of Genes Required for *Clostridium botulinum* Proliferation

30 Genes required for proliferation in *Clostridium botulinum* are identified according to the methods described above.

EXAMPLE 39

Identification of Genes Required for *Campylobacter jejuni* Proliferation

Genes required for proliferation in *Campylobacter jejuni* are identified according to the methods described above.

EXAMPLE 40

Identification of Genes Required for *Chlamydia trachomatis* Proliferation

5 Genes required for proliferation in *Chlamydia trachomatis* are identified according to the methods described above.

Use of Isolated Exogenous Nucleic Acid Fragments as Antisense Antibiotics

10 In addition to using the identified sequences to enable screening of molecule libraries to identify compounds useful to identify antibiotics, the sequences themselves can be used as therapeutic agents. Specifically, the identified exogenous sequences in an antisense orientation can be provided to an individual to inhibit the translation of a bacterial target gene.

Generation of Antisense Therapeutics from Identified Exogenous Sequences

15 The sequences of the present invention can be used as antisense therapeutics for the treatment of bacterial infections or simply for inhibition of bacterial growth *in vitro* or *in vivo*. The therapy exploits the biological process in cells where genes are transcribed into messenger RNA (mRNA) that is then translated into proteins. Antisense RNA technology contemplates the use of antisense oligonucleotides directed
20 against a target gene that will bind to its target and decrease or inhibit the translation of the target mRNA. In one embodiment, antisense oligonucleotides can be used to treat and control a bacterial infection of a cell culture containing a population of desired cells contaminated with bacteria. In another embodiment, the antisense oligonucleotides can be used to treat an organism with a bacterial infection.

25 Antisense oligonucleotides can be synthesized from any of the sequences of the present invention using methods well known in the art. In a preferred embodiment, antisense oligonucleotides are synthesized using artificial means. Uhlmann & Peymann, Chemical Rev. 90:543-584 (1990) review antisense oligonucleotide technology in detail. Modified or unmodified antisense oligonucleotides can be used as
30 therapeutic agents. Modified antisense oligonucleotides are preferred since it is well known that antisense oligonucleotides are extremely unstable. Modification of the phosphate backbones of the antisense oligonucleotides can be achieved by substituting

the internucleotide phosphate residues with methylphosphonates, phosphorothioates, phosphoramidates, and phosphate esters. Nonphosphate internucleotide analogs such as siloxane bridges, carbonate bridges, thioester bridges, as well as many others known in the art. The preparation of certain antisense oligonucleotides with modified internucleotide linkages is described in U.S. Patent No. 5,142,047, hereby incorporated by reference.

Modifications to the nucleoside units of the antisense oligonucleotides are also contemplated. These modifications can increase the half-life and increase cellular rates of uptake for the oligonucleotides *in vivo*. For example, α -anomeric nucleotide units and modified bases such as 1,2-dideoxy-d-ribofuranose, 1,2-dideoxy-1-phenylribofuranose, and N^4 , N^4 -ethano-5-methyl-cytosine are contemplated for use in the present invention.

An additional form of modified antisense molecules is found in peptide nucleic acids. Peptide nucleic acids (PNA) have been developed to hybridize to single and double stranded nucleic acids. PNA are nucleic acid analogs in which the entire deoxyribose-phosphate backbone has been exchanged with a chemically completely different, but structurally homologous, polyamide (peptide) backbone containing 2-aminoethyl glycine units. Unlike DNA, which is highly negatively charged, the PNA backbone is neutral. Therefore, there is much less repulsive energy between complementary strands in a PNA-DNA hybrid than in the comparable DNA-DNA hybrid, and consequently they are much more stable. PNA can hybridize to DNA in either a Watson/Crick or Hoogsteen fashion (Demidov et al., *Proc. Natl. Acad. Sci. U.S.A.* **92**:2637-2641, 1995; Egholm, *Nature* **365**:566-568, 1993; Nielsen et al., *Science* **254**:1497-1500, 1991; Dueholm et al., *New J. Chem.* **21**:19-31, 1997).

Molecules called PNA "clamps" have been synthesized which have two identical PNA sequences joined by a flexible hairpin linker containing three 8-amino-3,6-dioxaoctanoic acid units. When a PNA clamp is mixed with a complementary homopurine or homopyrimidine DNA target sequence, a PNA-DNA-PNA triplex hybrid can form which has been shown to be extremely stable (Bentin et al., *Biochemistry* **35**:8863-8869, 1996; Egholm et al., *Nucleic Acids Res.* **23**:217-222, 1995; Griffith et al., *J. Am. Chem. Soc.* **117**:831-832, 1995).

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The sequence-specific and high affinity duplex and triplex binding of PNA have been extensively described (Nielsen et al., *Science* **254**:1497-1500, 1991; Egholm et al., *J. Am. Chem. Soc.* **114**:9677-9678, 1992; Egholm et al., *Nature* **365**:566-568, 1993; Almarsson et al., *Proc. Natl. Acad. Sci. U.S.A.* **90**:9542-9546, 1993; Demidov et al., *Proc. Natl. Acad. Sci. U.S.A.* **92**:2637-2641, 1995). They have also been shown to be resistant to nuclease and protease digestion (Demidov et al., *Biochem. Pharm.* **48**:1010-1313, 1994). PNA has been used to inhibit gene expression (Hanvey et al., *Science* **258**:1481-1485, 1992; Nielsen et al., *Nucl. Acids. Res.*, **21**:197-200, 1993; Nielsen et al., *Gene* **149**:139-145, 1994; Good & Nielsen, *Science*, **95**: 2073-2076, 1998; all of which are hereby incorporated by reference), to block restriction enzyme activity (Nielsen et al., *supra.*, 1993), to act as an artificial transcription promoter (Mollegaard, *Proc. Natl. Acad. Sci. U.S.A.* **91**:3892-3895, 1994) and as a pseudo restriction endonuclease (Demidov et al., *Nucl. Acids. Res.* **21**:2103-2107, 1993). Recently, PNA has also been shown to have antiviral and antitumoral activity mediated through an antisense mechanism (Norton, *Nature Biotechnol.*, **14**:615-619, 1996; Hirschman et al., *J. Investig. Med.* **44**:347-351, 1996). PNAs have been linked to various peptides in order to promote PNA entry into cells (Basu et al., *Bioconj. Chem.* **8**:481-488, 1997; Pardridge et al., *Proc. Natl. Acad. Sci. U.S.A.* **92**:5592-5596, 1995).

The antisense oligonucleotides contemplated by the present invention can be administered by direct application of oligonucleotides to a target using standard techniques well known in the art. The antisense oligonucleotides can be generated within the target using a plasmid, or a phage. Alternatively, the antisense nucleic acid may be expressed from a sequence in the chromosome of the target cell. It is further contemplated that contemplated that the antisense oligonucleotide contemplated are incorporated in a ribozyme sequence to enable the antisense to specifically bind and cleave its target mRNA. For technical applications of ribozyme and antisense oligonucleotides see Rossi et al., *Pharmacol. Ther.* **50**(2):245-254, (1991), which is hereby incorporated by reference. The present invention also contemplates using a retron to introduce an antisense oligonucleotide to a cell. Retron technology is exemplified by U.S. Patent No. 5,405,775, which is hereby incorporated by reference. Antisense oligonucleotides can also be delivered using liposomes or by electroporation techniques which are well known in the art.

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laboratory animals. It is additionally contemplated that cells from the subject are removed, treated with the antisense oligonucleotide, and reintroduced into the subject. This range is merely illustrative and one of skill in the art are able to determine the optimal concentration to be used in a given case.

5 After the bacterial cells have been killed or controlled in a desired culture, the desired cell population may be used for other purposes.

EXAMPLE 41

10 The following example demonstrates the ability of an *E. coli* antisense oligonucleotide to act as a bactericidal or bacteriostatic agent to treat a contaminated cell culture system. The application of the antisense oligonucleotides of the present invention are thought to inhibit the translation of bacterial gene products required for proliferation.

15 The antisense oligonucleotide of this example corresponds to a 30 base phosphorothioate modified oligodeoxynucleotide complementary to a nucleic acid involved in proliferation, such as Molecule Number EcXA001. A sense oligodeoxynucleotide complementary to the antisense sequence is synthesized and used as a control. The oligonucleotides are synthesized and purified according to the procedures of Matsukura, et al., Gene 72:343 (1988). The test oligonucleotides are dissolved in a small volume of autoclaved water and added to culture medium to make a
20 100 micromolar stock solution.

 Human bone marrow cells are obtained from the peripheral blood of two patients and cultured according standard procedures well known in the art. The culture is contaminated with the K-12 strain of *E. coli* and incubated at 37°C overnight to establish bacterial infection.

25 The control and antisense oligonucleotide containing solutions are added to the contaminated cultures and monitored for bacterial growth. After a 10 hour incubation of culture and oligonucleotides, samples from the control and experimental cultures are drawn and analyzed for the translation of the target bacterial gene using standard microbiological techniques well known in the art. The target *E. coli* gene is found to be
30 translated in the control culture treated with the control oligonucleotide, however, translation of the target gene in the experimental culture treated with the antisense oligonucleotide of the present invention is not detected or reduced.

EXAMPLE 42

5 A subject suffering from an *E. coli* infection is treated with the antisense oligonucleotide preparation of Example 39. The antisense oligonucleotide is provided in a pharmaceutically acceptable carrier at a concentration effective to inhibit the translation of the target gene. The present subject is treated with a concentration of antisense oligonucleotide sufficient to achieve a blood concentration of about 100 micromolar. The patient receives daily injections of antisense oligonucleotide to maintain this concentration for a period of 1 week. At the end of the week a blood sample is drawn and analyzed for the presence or absence using standard techniques well known in the art. There is no detectable evidence of *E. coli* and the treatment is terminated.

EXAMPLE 43

Preparation and use of Triple Helix Probes

15 The sequences of microorganism genes required for proliferation of the present invention are scanned to identify 10-mer to 20-mer homopyrimidine or homopurine stretches that could be used in triple-helix based strategies for inhibiting gene expression. Following identification of candidate homopyrimidine or homopurine stretches, their efficiency in inhibiting gene expression is assessed by introducing varying amounts of oligonucleotides containing the candidate sequences into a population of bacterial cells that normally express the target gene. The oligonucleotides may be prepared on an oligonucleotide synthesizer or they may be purchased commercially from a company specializing in custom oligonucleotide synthesis, such as GENSET, Paris, France.

20 The oligonucleotides can be introduced into the cells using a variety of methods known to those skilled in the art, including but not limited to calcium phosphate precipitation, DEAE-Dextran, electroporation, liposome-mediated transfection or native uptake.

25 Treated cells are monitored for a reduction in proliferation using techniques such as monitoring growth levels as compared to untreated cells using optical density measurements. The oligonucleotides that are effective in inhibiting gene expression in cultured cells can then be introduced *in vivo* using the techniques well known in that art at a dosage level shown to be effective.

In some embodiments, the natural (beta) anomers of the oligonucleotide units can be replaced with alpha anomers to render the oligonucleotide more resistant to nucleases. Further, an intercalating agent such as ethidium bromide, or the like, can be attached to the 3' end of the alpha oligonucleotide to stabilize the triple helix. For information on the generation of oligonucleotides suitable for triple helix formation see Griffin et al. (*Science* 245:967-971 (1989), which is hereby incorporated by this reference).

EXAMPLE 44

Identification of Bacterial Strains from Isolated Specimens by PCR

Classical bacteriological methods for the detection of various bacterial species are time consuming and costly. These methods include growing the bacteria isolated from a subject in specialized media, cultivation on selective agar media, followed by a set of confirmation assays that can take from 8 to 10 days or longer to complete. Use of the identified sequences of the present invention provides a method to dramatically reduce the time necessary to detect and identify specific bacterial species present in a sample.

In one exemplary method, bacteria are grown in enriched media and DNA samples are isolated from specimens of, for example, blood, urine, stool, saliva or central nervous system fluid by conventional methods. A panel of PCR primers based on identified sequences unique to various species of microorganisms are then utilized in accordance with Example 12 to amplify DNA of approximately 100-200 bases in length from the specimen. A separate PCR reaction is set up for each pair of PCR primers and after the PCR reaction is complete, the reaction mixtures are assayed for the presence of PCR product. The presence or absence of bacteria from the species to which the PCR primer pairs belong is determined by the presence or absence of a PCR product in the various test PCR reaction tubes.

Although the PCR reaction is used to assay the isolated sample for the presence of various bacterial species, other assays such as the Southern blot hybridization are also contemplated.

All documents cited herein are incorporated herein by reference in their entireties.

WHAT IS CLAIMED IS:

1. A purified or isolated nucleic acid sequence consisting essentially of one of SEQ ID NOs: 405-485, wherein said nucleic acid inhibits microorganism proliferation.

2. The nucleic acid sequence of Claim 1, wherein said nucleic acid sequence is complementary to at least a portion of a coding sequence of a gene whose expression is required for microorganism proliferation.

3. The nucleic acid sequence of Claims 1 or 2, wherein said nucleic acid comprises a fragment of one of SEQ ID NOs. 405-485, said fragment selected from the group consisting of fragments comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.

4. The nucleic acid sequence of Claim 3, wherein said nucleic acid sequence is complementary to a coding sequence of a gene whose expression is required for microorganism proliferation.

5. A vector comprising a promoter operably linked to a nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs. 405-485.

6. The vector of Claim 5, wherein said promoter is active in an organism selected from the group consisting of *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *campylobacter jejuni*, *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

7. A host cell containing the vector of Claim 5 or Claim 6.

8. A purified or isolated nucleic acid consisting essentially of the coding sequence of one of SEQ ID NOs: 82-88, 90-242.

9. A fragment of the nucleic acid of Claim 8, said fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

10. A vector comprising a promoter operably linked to the nucleic acid of Claim 8 or Claim 9.

11. A purified or isolated nucleic acid comprising a nucleic acid sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region within an operon encoding a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

12. A purified or isolated nucleic acid comprising a nucleic acid having at least 70% homology to a sequence selected from the group consisting of SEQ ID NOs 405-485, 82-88, 90-242 or the sequences complementary thereto as determined using BLASTN version 2.0 with the default parameters.

13. The nucleic acid of Claim 12, wherein said nucleic acid is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus fumigatus*, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

14. A purified or isolated nucleic acid consisting essentially of a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

15. A vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

16. A host cell containing the vector of Claim 15.

17. A purified or isolated polypeptide comprising the sequence of one of SEQ ID NOs: 243-357, 359-398.

18. A purified or isolated polypeptide comprising a fragment of one of the polypeptides of SEQ ID NOs. 243-357, 359-398, said fragment selected from the group consisting of fragments comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the polypeptides of SEQ ID NOs.: 243-357, 359-398.

19. An antibody capable of specifically binding the polypeptide of Claim 17 or Claim 18.

20. A method of producing a polypeptide, comprising introducing a vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 into a cell.

21. The method of Claim 20, further comprising the step of isolating said protein.

22. A method of inhibiting proliferation comprising inhibiting the activity or reducing the amount of a polypeptide having a sequence selected from the group consisting of SEQ ID NOs. 243-357, 359-398 or inhibiting the activity or reducing the amount of a nucleic acid encoding said polypeptide.

23. A method for identifying compounds which influence the activity of a polypeptide required for proliferation comprising:

contacting a polypeptide having a sequence selected from the group consisting of 243-357, 359-398 with a candidate compound; and

determining whether said compound influences the activity of said polypeptide.

24. The method of Claim 23, wherein said activity is an enzymatic activity.

25. The method of Claim 23, wherein said activity is a carbon compound catabolism activity.

26. The method of Claim 23, wherein said activity is a biosynthetic activity.

27. The method of Claim 23, wherein said activity is a transporter activity.

28. The method of Claim 23, wherein said activity is a transcriptional activity.

29. The method of Claim 23, wherein said activity is a DNA replication activity.

30. The method of Claim 23, wherein said activity is a cell division activity.

31. A method for assaying compounds for the ability to reduce the activity or level of a polypeptide required for proliferation, comprising:

providing a target, wherein said target comprises the coding sequence of a sequence selected from the group consisting of SEQ ID NOs. 82-88, 90-242;

contacting said target with a candidate compound; and

measuring an activity of said target.

32. The method of Claim 31, wherein said target is a messenger RNA molecule transcribed from a coding region of one of SEQ ID. NOs.: 82-88, 90-242 and said activity is translation of said messenger RNA.

33. The method of Claim 32, wherein said target is a coding region of one of SEQ ID. NOs. 82-88, 90-242 and said activity is transcription of said messenger RNA.

34. A compound identified using the method of Claim 31.

35. A method for identifying compounds which reduce the activity or level of a gene product required for cell proliferation comprising the steps of:

expressing an antisense nucleic acid against a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

contacting said sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

36. The method of Claim 35, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

37. The method of Claim 36, wherein said cell is an *E. coli* cell.

38. The method of Claim 36, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus*

fumigatus, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

39. The method of Claim 35, wherein said antisense nucleic acid is transcribed from an inducible promoter.

40. The method of Claim 39, further comprising the step of contacting said cell with a concentration of inducer which induces said antisense nucleic acid to a sublethal level.

41. The method of Claim 40, wherein said sub-lethal concentration of said inducer is such that growth inhibition is 8% or more.

42. The method of Claim 40, wherein said inducer is isopropyl-1-thio- β -D-galactoside.

43. The method of Claim 35, wherein growth inhibition is measured by monitoring optical density of a culture growth solution.

44. The method of Claim 35, wherein said gene product is a polypeptide.

45. The method of Claim 35, wherein said gene product is an RNA.

46. The method of Claim 44, wherein said gene product comprises a polypeptide having a sequence selected from the group consisting of SEQ ID NOs.: 243-357, 359-398.

47. A compound identified using the method of Claim 35.

48. A method for inhibiting cellular proliferation comprising introducing a compound with activity against a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242 or with activity against the product of said gene into a population of cells expressing a gene.

49. The method of Claim 48, wherein said compound is an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 405-485, or a proliferation-inhibiting portion thereof.

50. The method of Claim 49, wherein said proliferation inhibiting portion of one of SEQ ID NOs. 405-485 is a fragment comprising at least 10, at least 20, at least

25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.

51. The method of Claim 48, wherein said compound is a triple helix oligonucleotide.

5 52. A preparation comprising an effective concentration of an antisense oligonucleotide comprising a sequence selected from the group consisting of SEQ ID NOs.: 405-485, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier.

10 53. The preparation of Claim 52, wherein said proliferation-inhibiting portion of one of SEQ ID NOs. 405-485 comprises at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 405-485.

15 54. A method for inhibiting the expression of a gene in an operon required for proliferation comprising contacting a cell in a cell population with an antisense nucleic acid, said cell expressing a gene corresponding to one of SEQ ID NOs.: 82-88, 90-242, wherein said antisense nucleic acid comprises at least a proliferation-inhibiting portion of said operon in an antisense orientation that is effective in inhibiting expression of said gene.

20 55. The method of Claim 54, wherein said antisense nucleic acid is complementary to a sequence of a gene comprising one or more of SEQ ID NOs.: 82-88, 90-242.

56. The method of Claim 54, wherein said antisense nucleic acid is a sequence of one of SEQ ID NOs.: 405-485, or a portion thereof.

25 57. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a plasmid which expresses said antisense nucleic acid into said cell population.

58. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a phage which expresses said antisense nucleic acid into said cell population.

30 59. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a sequence encoding said antisense nucleic acid into the chromosome of said cell into said cell population.

60. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a retron which expresses said antisense nucleic acid into said cell population.

61. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a ribozyme into said cell-population, wherein a binding portion of said ribozyme is complementary to said antisense oligonucleotide.

62. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by introducing a liposome comprising said antisense oligonucleotide into said cell.

63. The method of Claim 54, wherein said cell is contacted with said antisense nucleic acid by electroporation.

64. The method of Claim 54, wherein said antisense nucleic acid is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive bases of one of SEQ ID NOs: 82-88, 90-242.

65. The method of Claim 54 wherein said antisense nucleic acid is an oligonucleotide.

66. A method for identifying bacterial strains comprising the steps of:
providing a sample containing a bacterial species; and
identifying a bacterial species using a species specific probe having a sequence selected from the group consisting of SEQ ID NOs. 405-485, 82-88, 90-242.

67. A method for identifying a gene in a microorganism required for proliferation comprising:

(a) identifying an inhibitory nucleic acid which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;

(b) contacting a second microorganism with said inhibitory nucleic acid;

(c) determining whether said inhibitory nucleic acid from said first microorganism inhibits proliferation of said second microorganism; and

(d) identifying the gene in said second microorganism which is inhibited by said inhibitory nucleic acid.

68. A method for assaying a compound for the ability to inhibit proliferation of a microorganism comprising:

- (a) identifying a gene or gene product required for proliferation in a first microorganism;
- 5 (b) identifying a homolog of said gene or gene product in a second microorganism;
- (c) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said second microorganism;
- 10 (d) contacting said second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;
- (e) contacting the sensitized microorganism of step (d) with a compound; and
- 15 (f) determining whether said compound inhibits proliferation of said sensitized microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized microorganism.

69. The method of Claim 68, wherein said step of identifying a gene involved in proliferation in a first microorganism comprises:

- 20 introducing a nucleic acid comprising a random genomic fragment from said first microorganism operably linked to a promoter wherein said random genomic fragment is in the antisense orientation; and
- comparing the proliferation of said first microorganism transcribing a first level of said random genomic fragment to the proliferation of said first microorganism transcribing a lower level of said random genomic fragment,
- 25 wherein a difference in proliferation indicates that said random genomic fragment comprises a gene involved in proliferation.

70. The method of Claim 69, wherein said step of identifying a homolog of said gene in a second microorganism comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a database using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78 algorithm with the default parameters.

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71. The method of Claim 69, wherein said step of identifying a homolog of said gene in a second microorganism comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide by identifying nucleic acids which hybridize to said first gene.

5 72. The method of Claim 69, wherein the step of identifying a homolog of said gene in a second microorganism comprises expressing a nucleic acid which inhibits the proliferation of said first microorganism in said second microorganism.

73. The method of Claim 69, wherein said inhibitory nucleic acid is an antisense nucleic acid.

10 74. The method of Claim 69, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of said homolog.

75. The method of Claim 69, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding said homolog.

15 76. The method of Claim 69, wherein the step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence comprises directly contacting said second microorganism with said nucleic acid.

77. The method of Claim 69, wherein the step of contacting the second microorganism with a proliferation-inhibiting amount of said nucleic acid sequence comprises expressing an antisense nucleic acid to said homolog in said second microorganism.

20 78. A compound identified using the method of Claim 68.

79. A method of assaying a compound for the ability to inhibit proliferation comprising:

25 (a) identifying an inhibitory nucleic acid sequence which inhibits the activity of a gene or gene product required for proliferation in a first microorganism;

(b) contacting a second microorganism with a proliferation-inhibiting amount of said inhibitory nucleic acid, thus sensitizing said second microorganism;

30 (c) contacting the proliferation-inhibited microorganism of step (b) with a compound; and

(d) determining whether said compound inhibits proliferation of said sensitized second microorganism to a greater extent than said compound inhibits proliferation of a nonsensitized second microorganism.

5 80. The method of Claim 79, wherein said inhibitory nucleic acid is an antisense nucleic acid which inhibits the proliferation of said first microorganism.

81. The method of Claim 79, wherein said inhibitory nucleic acid comprises a portion of an antisense nucleic acid which inhibits the proliferation of said first microorganism.

10 82. The method of Claim 79, wherein said inhibitory nucleic acid comprises an antisense molecule against the entire coding region of the gene involved in proliferation of the first microorganism.

83. The method of Claim 79, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding the gene involved in proliferation of the first microorganism.

15 84. A compound identified using the method of Claim 79.

85. A method for assaying compounds for activity against a biological pathway required for proliferation comprising:

20 sensitizing a cell by expressing an antisense nucleic acid against a nucleic acid encoding a gene product required for proliferation in a cell to reduce the activity or amount of said gene product;

contacting the sensitized cell with a compound; and

determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of an nonsensitized cell.

25 86. The method of Claim 85, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

87. The method of Claim 86, wherein said cell is an *E. coli* cell.

30 88. The method of Claim 85, wherein said cell is from an organism selected from the group consisting of *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Enterobacter cloacae*, *Helicobacter pylori*, *Neisseria gonorrhoeae*, *Enterococcus faecalis*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Salmonella typhimurium*, *Saccharomyces cerevisiae*, *Candida albicans*, *Cryptococcus neoformans*, *Aspergillus*

fumigatus, *Klebsiella pneumoniae*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella choleraesuis*, *Staphylococcus epidermidis*, *Mycobacterium tuberculosis*, *Mycobacterium leprae*, *Treponema pallidum*, *Bacillus anthracis*, *Yersinia pestis*, *Clostridium botulinum*, *Campylobacter jejuni*, and *Chlamydia trachomatis*, *Chlamydia pneumoniae* or any species falling within the genera of any of the above species.

89. The method of Claim 85, wherein said antisense nucleic acid is transcribed from an inducible promoter.

90. The method of Claim 89, further comprising contacting the cell with an agent which induces expression of said antisense nucleic acid from said inducible promoter, wherein said antisense nucleic acid is expressed at a sublethal level.

91. The method of Claim 90, wherein said sublethal level of said antisense nucleic acid inhibits proliferation by 8% or more.

92. The method of Claim 90, wherein said agent is isopropyl-1-thio- β -D-galactoside (IPTG).

93. The method of Claim 91, wherein inhibition of proliferation is measured by monitoring the optical density of a liquid culture.

94. The method of Claim 85, wherein said gene product comprises a polypeptide having a sequence selected from the group consisting of SEQ ID NOs: 243-357, 359-398.

95. A compound identified using the method of Claim 85.

96. A method for assaying a compound for the ability to inhibit cellular proliferation comprising:

contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell;

contacting said cell with said compound; and

determining whether said compound reduces proliferation to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.

97. The method of Claim 96, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antisense nucleic acid to a gene or operon required for proliferation.

98. The method of Claim 96, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antibiotic.

99. The method of Claim 96, wherein said cell contains a temperature sensitive mutation which reduces the activity or level of said gene product required for proliferation of said cell.

100. The method of Claim 99, wherein said antisense nucleic acid is directed against the nucleic acid encoding the same functional domain of said gene product required for proliferation of said cell to which said antisense nucleic acid is directed.

101. The method of Claim 99, wherein said antisense nucleic acid is directed against the nucleic acid a different functional domain of said gene product required for proliferation of said cell than the functional domain to which said antisense nucleic acid is directed.

102. A compound identified using the method of Claim 96.

103. A method for identifying the pathway in which a proliferation-required nucleic acid or its gene product lies comprising:

expressing a sublethal level of an antisense nucleic acid directed against said proliferation-required nucleic acid in a cell;

contacting said cell with an antibiotic, wherein the biological pathway on which said antibiotic acts is known; and

determining whether said cell has a substantially greater sensitivity to said antibiotic than a cell which does not express said sublethal level of said antisense nucleic acid.

104. A method for determining the pathway on which a test compound acts comprising:

(a) expressing a sublethal level of an antisense nucleic acid directed against a proliferation-required nucleic acid in a cell, wherein the biological pathway in which said proliferation-required nucleic acid lies is known,

(b) contacting said cell with said test compound; and

(c) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said antisense nucleic acid.

105. The method of Claim 104, further comprising:

(d) expressing a sublethal level of a second antisense nucleic acid directed against a second proliferation-required nucleic acid in said cell, wherein said second proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

5 (e) determining whether said cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said second antisense nucleic acid.

106. A purified or isolated nucleic acid consisting essentially of one of SEQ ID NOs: 358, 399-402.

10 107. A compound identified using the method of Claim 23.

108. A compound which interacts with the gene or gene product of a nucleic acid comprising a sequence of one of SEQ ID NOs: 82-88, 90-242 to inhibit proliferation.

15 109. A compound which interacts with a polypeptide comprising one of SEQ ID NOs. 243-357, 359-398 to inhibit proliferation.

110. A compound which interacts with a nucleic acid comprising one of SEQ ID NOs: 358, 399-402 to inhibit proliferation.

**GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION OF E.
COLI**

Abstract of the Disclosure

5 The sequences of nucleic acids encoding proteins required for *E. coli*
proliferation are disclosed. The nucleic acids can be used to express proteins or portions
thereof, to obtain antibodies capable of specifically binding to the expressed proteins, and
to use those expressed proteins as a screen to isolate candidate molecules for rational drug
discovery programs. The nucleic acids can also be used to screen for homologous genes
10 that are required for proliferation in microorganisms other than *E. coli*. The nucleic acids
can also be used to design expression vectors and secretion vectors. The nucleic acids of
the present invention can also be used in various assay systems to screen for proliferation
required genes in other organisms as well as to screen for antimicrobial agents.

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012600

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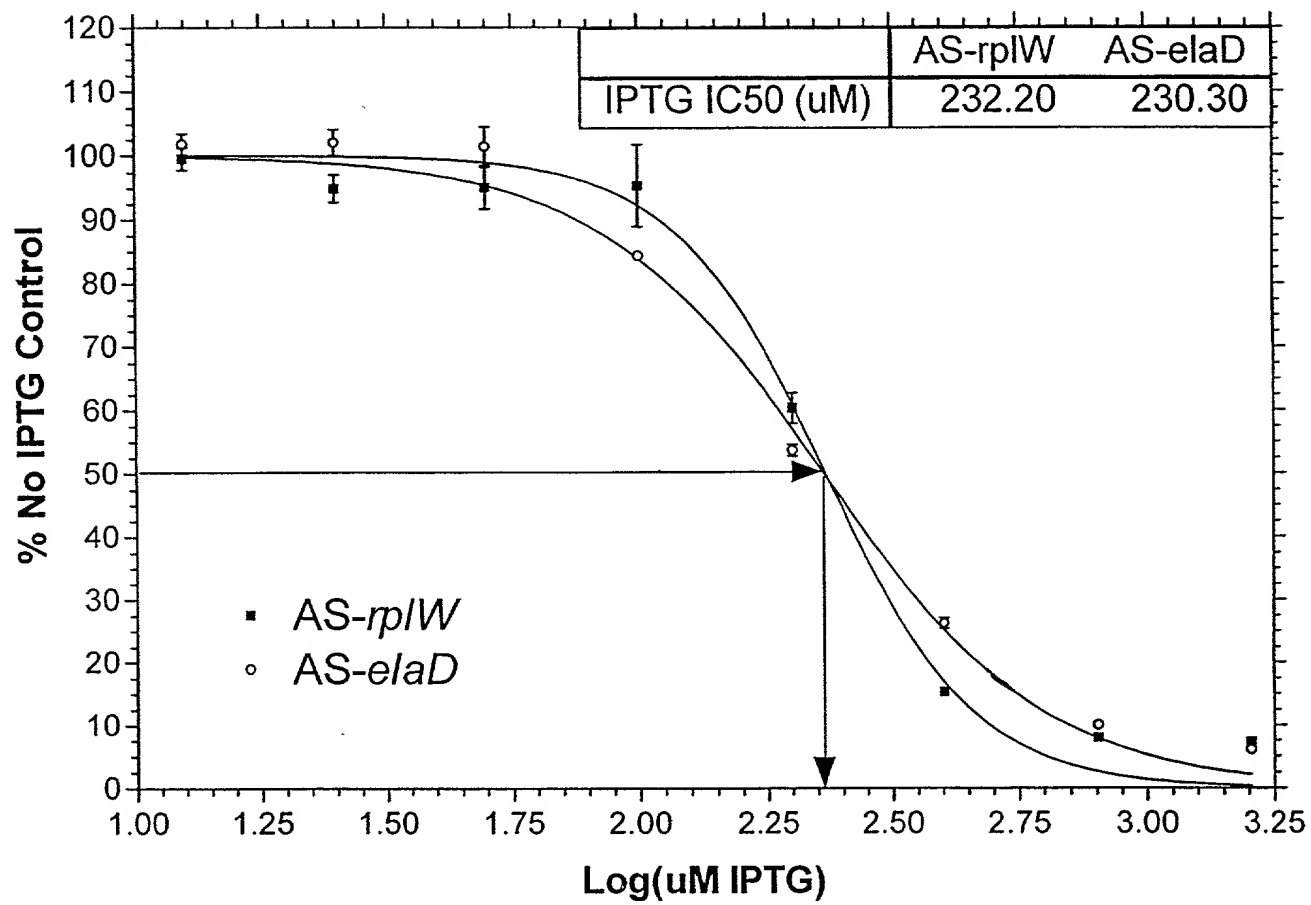


FIGURE 1

AS-rplW

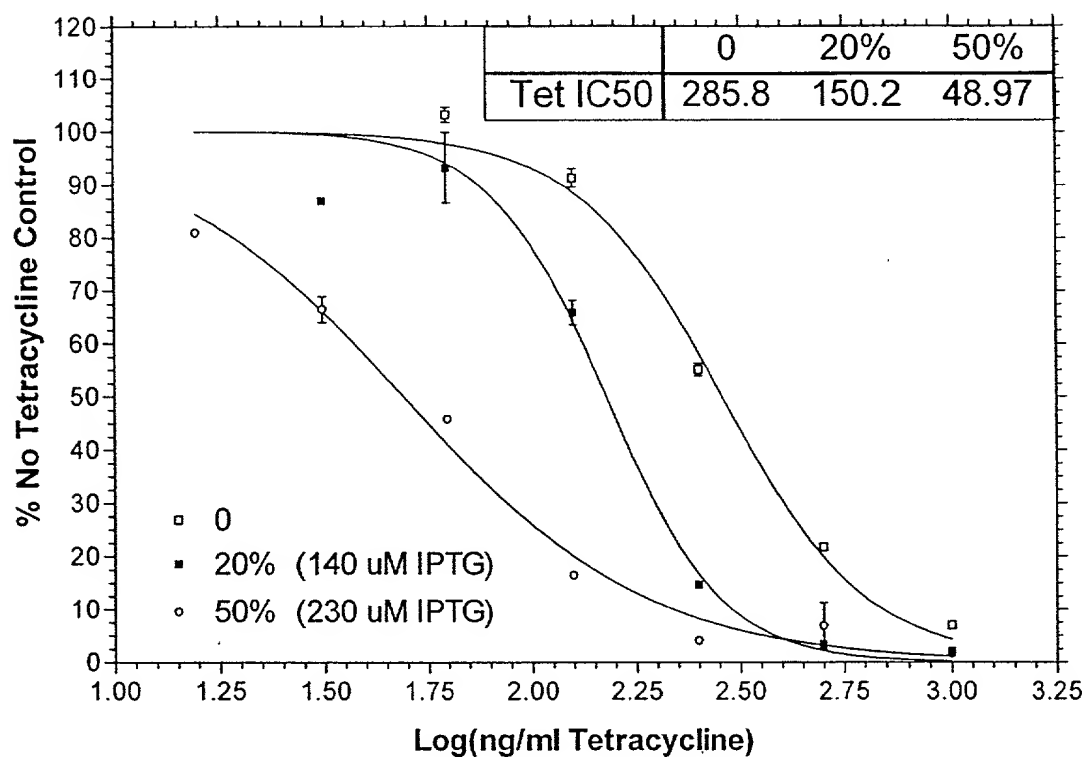


FIGURE 2a

AS-elaD

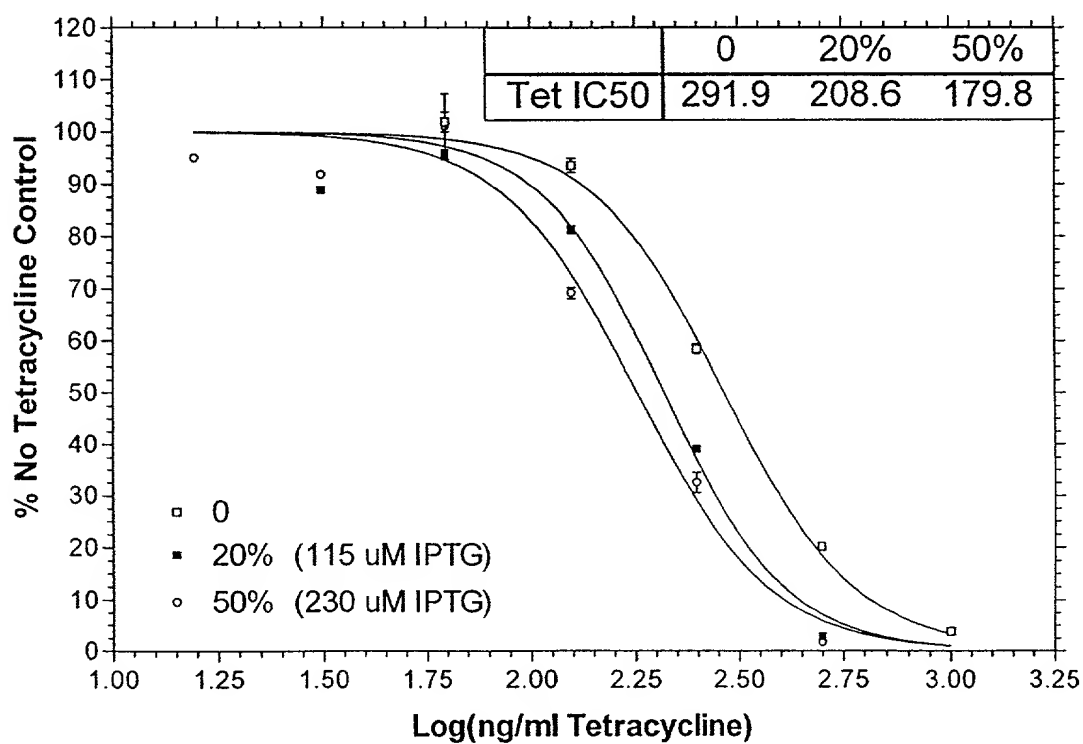


FIGURE 2b

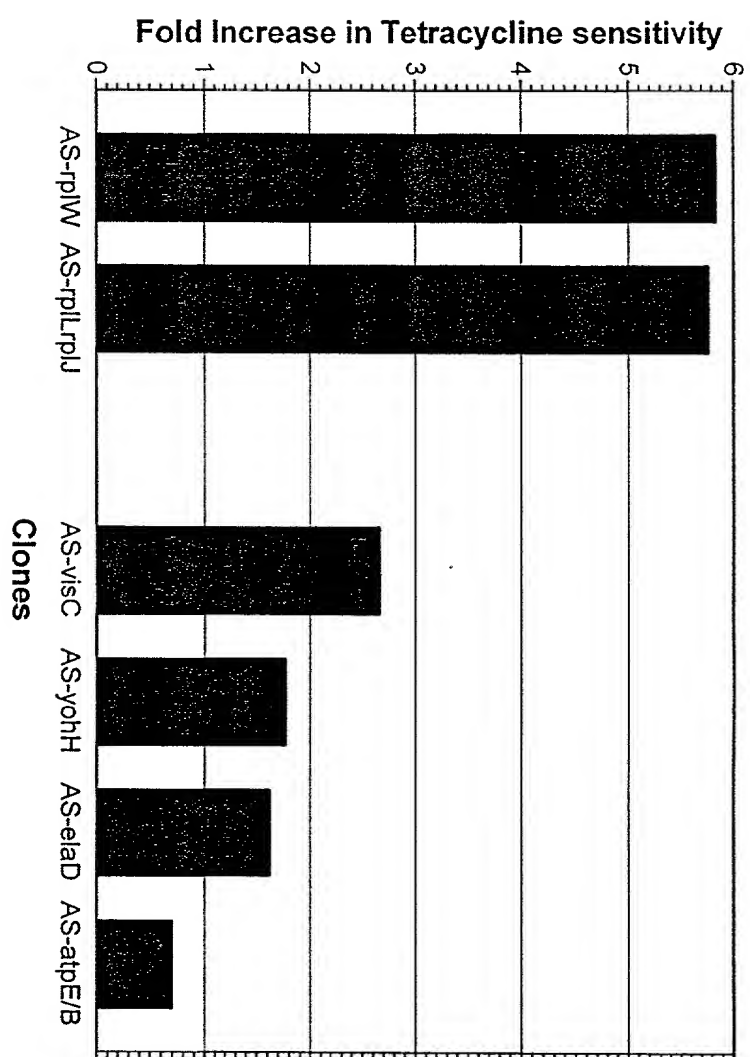


FIGURE 3 012300

SEQUENCE LISTING

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Ohlsen, Kari L.
Trawick, John
Forsyth, R. Allyn
Froelich, Jamie M.
Carr, Grant J.
Yamamoto, Robert T.
Xu, H. Howard

<120> GENES IDENTIFIED AS REQUIRED FOR PROLIFERATION IN
ESCHERICHIA COLI

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gggaggtctt	taacacgacc	gtcacggatc	aggatcacgg	agtgtctct		289

<210> 5
 <211> 815
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(815)
 <223> n = A,T,C or G

<400> 5

gggagcttac	atcagtaagt	gaccgggatg	agcagagcgaa	gataacgcat	ctgcggcgcg	60
aaatatgaag	ggggagagcc	cttatagacc	aggtagtaca	cgtttggtta	gggggcctgc	120
atatggcccc	ctttttcact	tttatatctg	tgcggtttta	tgccgggcag	atcacatctc	180
cgaggatttt	agaatggctg	aaattaccgc	atocctggta	aaagagctgc	gtgagcgtac	240
tggcgacggc	atgatggatt	gcaaaaaagc	actgactgaa	gctaacggcg	acatcgagct	300
ggcaatcgaa	aacatgcgta	agtcgggtgc	tattaaagca	gcgaaaaaag	caggcaacgt	360
tgctgctgac	ggcgtgatca	aaacccaaat	cgacggcaac	tacggcatca	ttctggaagt	420
taactgccag	actgacttcg	ttgcaaaaga	cgctggtttc	caggcgttcg	cagacaaagt	480
tctggacgca	gctgttgctg	gcaaaatcac	tgacgttgaa	gttctgaaag	cacagttcga	540
agaagaacgt	gttgogctgg	tagcgaaaat	tggtgaaaac	atcaacattc	gccgcgttgc	600
tgcgctggaa	ggcgacgttc	tgggttctta	tcagcacggg	gcgcgtatcg	gccgttctgg	660

ttgctgctaa aagcgctgac gaagaactgg ttaaacacat cgttttgacc tttgttgcaa	720
gccaaagccag aattcagaga aactttccgc ttcaccggag gtcccacca cangganccc	780
cgattttntc agcatggtgg tcttcctncg gagtt	815

<210> 6
 <211> 403
 <212> DNA
 <213> E. Coli

<400> 6	
caacactatt ttgttgaccg gaaaatggaa cactttccgc aatgcctgtt gctatcacgc	60
ttaaaccatt tcattgcatg ttacacagaa cggacgtcct gtgcgagtat attaatcgt	120
cgatagaaac aagcattgaa aggcacagca gtagtcaaac agtgtgaaac gctactggcg	180
ccttacagcg caaaaaggct ggtgactaaa aagtcaccag ccatcagcct gatttctcag	240
gctgcaaccg gaagggttgg cttattttaac ttcaacttca gcgccagctt cttccagagc	300
ttttttcagt gcttctgcgt cgtctttgct cagcctttct ttcagagcag ccggtgcaga	360
ttctaccagg tcttttagctt ctttcagacc caggccagtt gcg	403

<210> 7
 <211> 149
 <212> DNA
 <213> E. Coli

<400> 7	
gagctttttt cagtgtctct gcgtcgtctt tgctcacgcc ttctttcaga gcagccggtg	60
cagattctac caggtcttta gcttctttca gaccaggcc agttgcgcca cgtactgctt	120
tgataacagc aactttgtta gcgccagca	149

<210> 8
 <211> 742
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(742)
 <223> n = A,T,C or G

<400> 8	
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actttccgca atgcctgttg ctatcacgct taaaccattt cattgcgatt tacacagaac	120
ggacgtcctg tcgcagttata ttaagtcgtc gatagaaaca agcattgaaa ggcacagcag	180
tagtcaaaca gtgtgaaacg ctactggcgc cttacagcgc aaaaaggctg gtgactaaaa	240
agtcaccagc catcagcctg atttctcagg ctgcaaccgg aagggttggc ttattttaact	300
tcaacttcag cgccagcttc ttccagagct tttttcagtg cttctgcgtc gtctttgctc	360
acgccttctt tcagagcagc cgggtgcagat tctaccaggc ctttagcttc tttcagaccc	420
aggccagttg cgccacgtac tgctttgata acagcaactt tgttagcgcc agcagctttc	480
agaattacgt cgaattcagt tntttcttca gcagcttcaa ccggggccagc agctacagct	540
acagcagcag caagcggaaa caccgaattt ttcttccatt gcagagatca gttctacaac	600
cgtccattac agacatagct gcaactgctt caatgatctt gatctttagt ggatagacat	660
ttaaattgtt cctgaattat caagaaataa gtntttatag taagccgaaa tgcgttaaaa	720
aagataactg ngattaaaagc ag	742

<210> 9
 <211> 421
 <212> DNA
 <213> E. Coli

<400> 9
agtagtcaaa cagtgtgaaa cgctactggc gccttacagc gcaaaaaggc tggtagactaa 60
aaagtcacca gccatcagcc tgattttctca ggctgcaacc ggaagggttg gcttatttaa 120
cttcaacttc agcgccagct tcttccagag cttttttcag tgcttctgcg tctgtctttgc 180
tcacgccttc tttcagagca gccggtgcag attctaccag gtcttttagct tctttcagac 240
ccaggccagt tgcgccacgt actgctttga taacagcaac tttgttagcg ccagcagctt 300
tcagaattac gtcgaattca gttttttctt cagcagcttc aaccgggcca gcagctacag 360
ctacagcagc agcagcggaa acaccgaatt tttcttccat tgcagagatc agttctacaa 420
c 421

<210> 10
<211> 126
<212> DNA
<213> E. Coli

<400> 10
agagcttttt tcagtgtctt tgcgtcgtct ttgctcacgc cttcttttcag agcagccggt 60
gcagattcta ccagggtctt agcttctttc agaccaggc cagttgcgcc acgtactgct 120
ttgata 126

<210> 11
<211> 262
<212> DNA
<213> E. Coli

<220>
<221> misc_feature
<222> (1)...(262)
<223> n = A,T,C or G

<400> 11
ctgcaaccgg aagggttggc ttattttaact tcaacttcag cgccagcttc ttccagagct 60
tttttcagtg cttctgcgtc gtctttgctc acgccttctt tcagagcagc cgntgcagat 120
totaccaggt ctttagcttc tttcagaccc aggccagttg cgccacgtac tgctttgata 180
acagcaactt tgtttagcgc agcagctttc agaattacgt cgaattcagt tttttcttca 240
gcagcttcaa ccgggccagc ag 262

<210> 12
<211> 202
<212> DNA
<213> E. Coli

<220>
<221> misc_feature
<222> (1)...(202)
<223> n = A,T,C or G

<400> 12
gcgcatacc tgcagcatcg gccgatgga gatcaggctg gcagaacgct gtaccgcttt 60
gtaggtggtg ttaccggtgn tcagatccgg gaagatgaac acggtagcgc gacctgcaac 120
cggagagttc ggcgctttgg attnccgaac gtcagccatt accgcagcgt cgtactgcag 180
cggaccggcg atcatcaggt ca 202

<210> 13
<211> 261
<212> DNA

<213> E. Coli

<400> 13

tctaggagta	agaatagctt	caaattcagc	agttgacagt	ggcataaacg	taactggtga	60
cttttgcccg	gcatgacgcc	gggctttttt	tattattccg	tgacttccag	cgtagtgaag	120
gcaaacttct	cgccatcaaa	tagccccctg	ctgggttagt	ttagcgcggg	gatcactggc	180
agagaaagaa	acgccatctg	aataaacggc	tcatcgggta	acggaccgca	ttcacgggcg	240
gcggctttca	aggcgtaaat	t				261

<210> 14

<211> 224

<212> DNA

<213> E. Coli

<400> 14

ttotTTTTTT	cgTcaacggT	gtccagaatc	attttatttT	cctcggggta	cttatgctga	60
tttttattat	tatggggaag	gtgttatttT	tgagtttcat	ttatgccgta	acgacaatga	120
actcggaat	tagtataagc	agcgogagaa	taataatcat	tgtgcaaatg	ctaatttaat	180
taatactatt	taaatattat	tttgagcata	tgacataag	gttg		224

<210> 15

<211> 232

<212> DNA

<213> E. Coli

<400> 15

aattcccttc	TTTTTTTcgt	caacggTgtc	cagaatcatt	ttattttacct	cgggtactta	60
tgctgatttt	tattattatg	gggaaggTgt	tatttatgag	tttcatttat	gccgtaacga	120
caatgaactc	gggaattagt	ataagcagcg	cgagaataat	aatcattgtg	caaatgctaa	180
tttaattaat	actattttaa	tattattttg	agcatatgca	cataaggttg	gg	232

<210> 16

<211> 212

<212> DNA

<213> E. Coli

<400> 16

aatagcgggt	atgcacgcct	ttotTTTTTT	cgTcaacggT	gtccagaatc	attttatttT	60
cctcgggTac	ttatgctgat	ttttattatt	atggggaagg	tgttatttat	gagtttcatt	120
tatgccgtaa	cgacaatgaa	ctcggggaatt	agtataagca	gcgcgagaat	aataatcatt	180
gtgcaaatgc	taattttaatt	aatactatTT	aa			212

<210> 17

<211> 433

<212> DNA

<213> E. Coli

<400> 17

ccttgtaaAT	tatcgcccgT	ggcataaaaa	ctgcgtccaa	acgccgtctt	tgccagcagc	60
caggccataa	atgccaccag	aattatcgTc	aaccaaccaa	ttgctgaaac	gccaagcagc	120
agcggggcg	agagctgttt	cagttcggcg	ggtaaccctt	caatccattt	gccgccagtc	180
cacagcaaca	tgatgcctct	gtacaaccct	aacgtgccaa	gggtggcaac	aatggcagg	240
atctttagcc	acgcgaccag	gacaccgttg	aaaaatcccg	cgagcaaacc	aagcagtaaa	300
gtcgcgacac	aagcaacagg	tagtgaatat	cctgcgttca	gtaacatccc	caacagcacc	360
gcgcacattc	cggtaatcga	acccactgaa	acatcaatat	tgccgcgtaag	cattaccagc	420
gtcgcgcCCA	ttg					433

<210> 18
 <211> 658
 <212> DNA
 <213> E. Coli

<400> 18
 cgtgcgcttc cggttgtggc aacccgcgaa atggcgcggc ggtaagtatg gcgggggttat 60
 tccttccccg ttgaggacac cgggttgtca ggttgaccat acgcttaagt gacaacccccg 120
 ctgcaacgcc ctctgttata aattttctgg tgacgtttgg cggtatcagt tttactccgt 180
 gaotgotctg ccgccctttt taaagtgaat tttgtgatgt ggtgaatgcg gctgagcgca 240
 cgcggaacag ttaaaaccaa aaacagtgtt atgggtggat tctctgtatc cggcgtaaat 300
 tgtaaactgg ttaacgtcac ctggaggcac caggcactgc atcacaaaat tcattgttga 360
 ggacgcgata atgaaaacgt tattaccaaa cgtaataacg tctgaagggt gttttgaaat 420
 tgggtgtcact atcagtaacc cagtattttac tgaagatgcc attaacaaga gaaaacaaga 480
 acgggagcta ttaataaaaa tatgcattgt ttcaatgctg gctcgtttac gtctgatgcc 540
 aaaaggatgt gcacaatgaa ttcagcattt gtgcttgctt tgacagtttt tcttggttcc 600
 ggagagccag ttgatattgc agtcaagtgg tcacaggaca atgcaggagt gtatgact 658

<210> 19
 <211> 588
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(588)
 <223> n = A,T,C or G

<400> 19
 gtgactgctc tgccgccctt tttaaagtga attttgtgat gtggtgaatg cggctgagcg 60
 cacgcggaac agttaaaacc aaaaacagtg ttatgggtgg attctctgta tccggcggtta 120
 attgttaact ggttaacgtc acctggaggc accaggcact gcatcacaaa attcattgtt 180
 gaggacgcga taatgaaaac gttattacca aacgttaata cgtctgaagg ttgttttgaa 240
 attggtgtca ctatcagtaa ccagtatatt actgaagatg ccattaacaa gagaaaacaa 300
 gaacgggagc tattaataaa aatatgcatt gtttcaatgc tggctcgttt acgtctgatg 360
 ccaaaaggat gtgcacaatg aattcagcat ttgtgcttgt tctgacagtt tttcttggtt 420
 ccggagagcc agttgatatt gcagtcagtg ttcacaggac aatgcangag tgtatgactg 480
 cagcaacccg aacagaaaat tcccggtaac tgttacccgg tcgataaagt tattcaccag 540
 gataatatcg aaatcccggc aggtctttta aacagttccg taataaat 588

<210> 20
 <211> 101
 <212> DNA
 <213> E. Coli

<400> 20
 gatccagcaa gaagatgcgg ttgtacogtc atcacgcaga tgcgcaaagc tactcagcaa 60
 ctgacctttc ttcgcaataa gcacgccatt agcgtcatag a 101

<210> 21
 <211> 465
 <212> DNA
 <213> E. Coli

<400> 21
 tcgctgtttt accttcaaca tcggttaact tctggcggat agtttcacgg taagcaacct 60
 gcggtttacc tacgttcgct tcaacgttga attcacgctt catacgggtca acgatgatgt 120

cgaggtgcag	ttcgcccata	cccgcgatga	tggtctgggt	agattcttcg	tcagtccata	180
cacggaaaga	cgggtcttct	ttagccagac	ggcccagagc	cagaccatt	ttttcctggt	240
cagctttggt	tttcggttca	actgcgatgg	agattaccgg	ctcaggaat	tccatacgtt	300
ccagaatgat	cggcgcaccc	gggtcacaca	gggtgtcacc	agtggttacg	tttttcagac	360
cgatagcagc	agcgatgtcg	cccgcgcgaa	cttctttgat	ctcttcacgt	ttgttagcgt	420
gcattctgaac	gatacgaccg	aaacgctcac	gtgcagcttt	cacgg		465

<210> 22
 <211> 859
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(859)
 <223> n = A,T,C or G

<400> 22						
tgatcggtc	aagcagaact	ggtttcgctt	tcttaaagcc	ttctttaaag	gcgatagaag	60
cagccagttt	aaacgccagt	tcagaggagt	caacgtcatg	gtaagaaccg	aagtgcagac	120
gaatacccat	gtctactacc	gggtagcctg	ccagcggacc	tgctttcagc	tgttcctgga	180
tacctttatc	aacggccggg	atgtattcgc	cagggattac	accaccttta	atgtcgttga	240
tgaactcgta	gcctttcggg	tttgaacccg	gctccagcgg	gtacatgtcg	ataacaacat	300
gaccatactg	accacgacca	ccagactggt	tcgcgtgttt	accttcaaca	tcggtaactt	360
tctggcggat	agtttcacgg	taagcaacct	gcggtttacc	tacgttcgct	tcaacgttga	420
attcacgctt	catacggtea	acgatgatgt	cgaggtgcag	ttcgcccata	cccgcgatga	480
tggtctgggt	agattcttcg	tcagtccata	cacggaaaga	cgggtcttct	ttagccagac	540
gggccanagc	cagaccatt	ttttcctggt	cagctttggt	tttcggtcaa	ctgcgatgga	600
gattaccggc	tcanggaatt	tccatacctt	ccaggaatga	tcggcgcatt	ccggtcaaac	660
angngtacc	aggggggtac	ntntttttta	nancgattgc	cagcancgga	tntnncccg	720
gccnaacttc	tttggaaacn	tttaccgggt	ggtaaccngc	cttttnaach	atccaaccga	780
aaaagngtta	anngccantt	ttcengngt	tnanntnccg	nttcccngaa	ntaaccnc	840
cgggtgnaac	cngnaaaa					859

<210> 23
 <211> 269
 <212> DNA
 <213> E. Coli

<400> 23						
ctttcttaaa	gccttcttta	aaggcgatag	aagcagccag	tttaaaccgc	agttcagagg	60
agtcaacgtc	atggttaagaa	ccgaagtga	gacgaatacc	catgtctact	accgggtagc	120
ctgccagcgg	acctgctttc	agctgttcct	ggataccttt	atcaacggcc	gggatgtatt	180
cgccagggat	tacaccacct	ttaatgtcgt	tgatgaactc	gtagcctttc	gggtttgaac	240
ccggtccag	cgggtacatg	tcgataaca				269

<210> 24
 <211> 330
 <212> DNA
 <213> E. Coli

<400> 24						
gttttgggga	gatgtaaggg	ctaactctgaa	tggtgcatt	ccttgtttaa	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tgttttacag	120
ctgactcttc	tgttcttata	acacaaggaa	acgtacttaa	ggtgogtccg	gtgaaccagt	180
cggacgcacc	tttaataact	ataaataagt	gtctgggcag	atactatata	aattaactta	240
gtgaatgatt	atgctaattg	catcaattaa	ataaatataa	tggcgttaag	gcttcccagt	300

aatataatta atactctact tccagagtag

330

<210> 25

<211> 471

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(471)

<223> n = A,T,C or G

<400> 25

gttttgggga	gatgtaaggg	ctaactctgaa	tggctgcatt	ccttgtttaa	ggaaaaacga	60
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ctgatccttc	tgttcttata	acacaaggaa	acgtacttaa	ggcgccgtcc	ggatgaaccag	180
tcggagcgac	ctttaataac	tataaataag	tgtctgggca	gatactatat	aaattaactt	240
agtgaatgat	tatgctaata	tcattcaatta	aataaatata	atggcggtta	ggcttcccag	300
taatataatt	aatactctac	ttccagagta	gaatattaaa	ttttatccgc	gtgggtgcac	360
agcacaaatt	tatcccacaa	ctgttcttct	gtctcgacat	gccccccgat	ctttnacaaa	420
tantattggg	ggattngggc	cncctttttg	ncaggttggg	gtcctctnat	g	471

<210> 26

<211> 379

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(379)

<223> n = A,T,C or G

<400> 26

natctgantg	gctgcattcc	ttgtttaagg	aaaccogaat	gactgattgc	cgatacctga	60
ttaaacgggt	catcaaaaac	atcattgctg	ttttacagct	gacccctctg	ttcttataac	120
acaaggaaac	gtacttaagg	tgcgtccggt	gaaccagtcg	gacgcacctt	taataactat	180
aaataagtgt	ctgggcagat	actatataaa	tttaacttagt	gaatgattat	gctaagtgtc	240
tcaattaaat	aaatataatg	gcgttaaggc	ttcccagtaa	tataattaat	actctacttc	300
cagagtagaa	tattaaattt	tatccgcgtg	gtgcatcagc	acaaatttat	cccacaactg	360
ttcttctgtc	tcgacatgc					379

<210> 27

<211> 799

<212> DNA

<213> E. Coli

<400> 27

aaagatgatg	tgatgagaaa	gtcaattttga	ataagacaat	attaagagct	aaaaaaatgt	60
caaaaaacac	taaatcaaaa	aataatggca	ttagaaaaata	taatgcgaaa	acggaggtga	120
aattagttta	tttcaaatga	ggaaaatctc	ccggcgaaaa	aaccgggaga	tgaaagtgtg	180
atgggtatca	aataaacaac	agaggagaaa	tttttaacgc	agccattcag	gcaaactcgtt	240
taatcccatt	gcctggcgga	taagttgcgg	cttaacgcc	ggaagcgtgt	cggccagttt	300
caaaccaata	tcacgcagca	gttttttcgc	cggattggta	ccggaaaaca	gatcgcggaa	360
tccttgcata	ccagccagca	tcaacgcgc	actgtgcttg	cggctacgct	catagcgacg	420
cagataaatg	tactgcccga	tgtctgggat	ccgtcgacct	gcagccaagc	ttgggctttt	480
cagcctgata	cagattaaat	cagaacgcag	aagcggctctg	ataaaacaga	atttgcctgg	540
cggcagtagc	gcggtgggtcc	cacctgacct	catgccgaac	tcagaagtga	aacgcccgtg	600

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gcgcccgatg gtagtggtggg gtctcccat gcgagagtag ggaactgcca ggcatacaat 660
aaaacgaaag gctcagtcga aagactgggc ctttcggttt atctggtggt tgcgggtgaa 720
cgctctctga gtaggacaaa tccgccggga gcggattttg aacgttgcca aacaaccggc 780
ccggaaaggg gtgggggct

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<210> 28
<211> 636
<212> DNA
<213> E. Coli

```

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<220>
<221> misc_feature
<222> (1)...(636)
<223> n = A,T,C or G

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```

<400> 28
agggggtttg ttgtgggcaa tgatgcattt aagttatcgt ctgcagatag aggagatatt 60
acaataaaca acgaatcagg gcatttgata gtcaataccg caattctatc aggagatata 120
gtcactctaa gaggaggaga aattagggtt gtattatagc ttgtgcgcgc catgattggc 180
gcgcaattta aacttagtgc ttacatcgc tattgtcttg atttctttga attattttat 240
aaattaaaaa aacgactgtt atgtataagc aaaggtcgaa cgaaaaatac attccaaata 300
aatgottgct taaatctcta tatccttccc cgaaaaatga cacataaaat tgagatattc 360
caaaaagaga tactacaaat aaagatgcct ttatttttatt atttctaata aaaatagaag 420
caataaaaaa taataacaat gatataaatc taatgttttt aaatatattg tcttttatgt 480
tagtaatagt cgtagtatg tttgattctc catatattac gtgtagtttt ttatatacat 540
ggaaataatt ntctttatac tgagacatca caccatcatc aaatggaagt ttgaagatgg 600
tgcttggttt gctaaccaat aaaaagagtg cattcg
636

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```

<210> 29
<211> 757
<212> DNA
<213> E. Coli

```

```

<220>
<221> misc_feature
<222> (1)...(757)
<223> n = A,T,C or G

```

```

<400> 29
cagcggtcgt atttttagca tgggttttta ttggcggtta tgctgccccg ggagcataaa 60
gatgaaaaaa acaacgatta ttatgatggg tgtggcgatt attgtcgtac tcggcactga 120
gctgggatgg tggtaacgtc acctctaaaa aatagcaaag gctgcctgtg tgcagccttt 180
gtgcaattta agcgttaact tttaatcttc ctgtagataa atagcacgac aatcgacca 240
ataacggcaa ccacgaagct gccaaaattg aagccatcga ctttaccaaa gccaaacagc 300
gtgctgatcc atccgccgac tacggcaccg actatcccca gcaggatagt cataaagaat 360
ccacctccat ctttacctgg catgatccac ttogccagaa taccggcaat aagcccaaaa 420
ataatccatg acagaatgcc cattgtttcc tcacttatct gttttgcatt agcgggttag 480
tcgctgataa aaagcatagc acaacatcgg gagggcaaga tttgtgacga gcatcacgga 540
ggtttttttt gcgatggcgc agaaattgcg ccatcaacga tcagtataa ttaccaacca 600
caaacatcat gttcgttttc cgtgtcataa gaaccgtacg ggattcacca gatcttttat 660
cacttcaagc cggcacttct ggaccagca aagtcacggt cgtctctggt tcataatcga 720
ccggaaaacgc cattgctggt attggtgacn gtcacgg
757

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<210> 30
<211> 392
<212> DNA
<213> E. Coli

```


tcacgtggt gctcttagtc ataagcttcc ccgcttacta agactaccag ggcgggggaa 240
 accccgctct accctcactc ctgaaagtat gccttcacga taagattgtc aat 293

<210> 34
 <211> 633
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(633)
 <223> n = A,T,C or G

<400> 34
 atttacactt tttacgaaat catgggatca ctaacaaaat atcgcttgct agttatattg 60
 tatggcagga aagatatgcg actgatatta cagatcccca aagtggagag tttatgacca 120
 ttaaaaataa gatgttgctg ggtgcgcttt tgctgggttac cagtgcgcgc tgggcgcgcac 180
 cagccaccgc gggttcgacc aatacctcgg gaattttctaa gtatgagtta agtagtttca 240
 ttgctgactt taagcatttc aaaccagggg acaccgtacc agaaatgtac cgtaccgatg 300
 agtacaacat taagcagtgg cagttgcgta acctgcccgc gcctgatgcc gggacgcact 360
 ggacctatat ggggtggcgcg tacgtgttga tcagcgacac cgacggtaaa atcattaaag 420
 cctacgacgg tgagattttt tatcatcgct aaaaaaagcc ccctcatcat gagggggaaa 480
 tgcagacacc ttgntatttt ttattattag ccacttgctc gtcttgcttg gtattaagtc 540
 gtatttcacg ttgattaatg cnggtggctc cagtgcgcca gattaacttt gtttggatcg 600
 aagacgtagt aactggctgg ttatcggaat tgg 633

<210> 35
 <211> 569
 <212> DNA
 <213> E. Coli

<400> 35
 tatggcagga aagatatgcg actgatatta cagatcccca aagtggagag tttatgacca 60
 ttaaaaataa gatgttgctg ggtgcgcttt tgctgggttac cagtgcgcgc tgggcgcgcac 120
 cagccaccgc gggttcgacc aatacctcgg gaattttctaa gtatgagtta agtagtttca 180
 ttgctgactt taagcatttc aaaccagggg acaccgtacc agaaatgtac cgtaccgatg 240
 agtacaacat taagcagtgg cagttgcgta acctgcccgc gcctgatgcc gggacgcact 300
 ggacctatat ggggtggcgcg tacgtgttga tcagcgacac cgacggtaaa atcattaaag 360
 cctacgacgg tgagattttt tatcatcgct aaaaaaagcc ccctcatcat gagggggaaa 420
 tgcagacacc ttgttatttt ttattattag ccacttgctc gtcttgcttg ttattagtcg 480
 tatttcacgt tgattaatgc ggttgccctc agtgcgcccag atttaacttt gtttgtatcg 540
 tagacgtagt aactggctgg tatcggaat 569

<210> 36
 <211> 338
 <212> DNA
 <213> E. Coli

<400> 36
 cgtattcaca tccttttgat tggtgataac atgcgaatcg gtattatttt tccggttgta 60
 atcttcatta cagcggctcg attttttagca tggtttttta ttggcgggta tgetgcccgc 120
 ggagcataaa gatgaaaaaa acaacgatta ttatgatggg tgtggcgatt attgtcgtac 180
 tcggcactgc ctgggatggg ggtaacgtca cctctaaaaa atagcaaagg ctgcctgtgt 240
 gcagcctttg tgcaatttaa gcgttaactt ttaatcttcc tgtagataaa tagcacgaca 300
 atcgcaccaa taacggcaac cacgaagctg ccaaaatt 338

<210> 37

[illegible]

ctgaatat	ttt	aaaaaggaaa	acgacatgaa	accgaagcac	agaatcaaca	ttctccaatc	60
ataaaatatt	tccgtggagc	at	ttttattat	tgaatataga	ggtttaactc	cggtaaaaaa	120
caaagaagca	ttgaatgcag	ggaaaaataa	tatggccata	aaaaacatcg	aaagaaactc		180
ttttaattta	acatgtaaac	gcatggttaa	tcctcatatc	acgggtggag	tgttaagaac		240
atacataaat	ggagtcatgt	tttccctttt	ccatttatca	agttcctggt	gccgttttag		300
tccatctcta	attgcatatt	ttaat	tttttc	tgataaatgg	cattgagcat	cgatttcatt	360
taaaacaact	gtaca						375

ttacgatagtc	tattagtaaa	aatataagag	ttagctgtat	tgttatgtct	gtggcgaaat	60
tgactacctt	cgtttttttg	attaagaatg	attttattat	cgtaagtaaa	attacatgaa	120
tatttaaaaa	ggaaaacgac	atgaaaaccga	agcacagaat	caacattctc	caatcataaa	180
atatttcctg	ggagcatttt	attattgaat	atagaggttt	aactccggtg	aaaaacaaag	240
aagcattgaa	tgcagggaaa	aataatatgg	ccataaaaaa	catcgaaaga	aactctttta	300
atttaacatg	taaacgcatg	gttaatcctc	atatcacggg	tggagtgtta	agaacataca	360
taaatggagt	catgttttcc	cttttccatt	tatcaagttc	ctgttgccgt	tttagtccat	420
ctctaattgc	atattttaat	ttttct				446

<223> n = A, T, C or G

tcaccccggt	gcgattttc	aggcatcctg	atttaactta	gcacccgcaa	cttaactaca	60
ggaaaacaaa	gagataaatg	tctaatectg	atgcaaactg	agccgatttt	ttaatcttta	120
cggaactttta	ccgcctggt	ttattaattg	cactgtnatc	cgggcggttcg	cccgttttaa	180
tcacaatagg	ctgtgtagcc	tgggcctggt	tctctttcac	ccgcgcacaga	gcggcgacaa	240
tgcactcttt	atctttggct	gcaggttgaa	cggtgcgct	cttatgtcgt	tcaaggcgag	300
cgcctttttc	gcgctccaga	cgagcctggc	gcgcttcgaa	acgcgccttg	gcttctgcgg	360
cncgcctttc	ttcctgacga	atagccgcaa	tt			392

taataacgct	atctgcggat	aaagcagaat	aggtgggttaa	cccagacat	aaaccgagga	60
aaataatggt	attgtatttc	ataatctatt	gttccttagc	gacagattgc	tgtctgctgg	120
ttcagtaagg	taccaggaga	aacttcagga	agcttgtaact	cgacaataca	gtttgagttt	180
ttatctttgc	cccatgaaac	ctgtaatt				208

<210> 41
 <211> 342
 <212> DNA
 <213> E. Coli

<400> 41
 catcctcaat accgttaaatt gcaacccgaa cccccgttgt ccctttgctg cattcaactta 60
 acgtaatctg aaaagggacg gctggacttg tgctaccggt cgttggaaat tgtctggcac 120
 tgtttttttg gagatctacg gtaaaattaa gcgaatccga tgagactgtg cagccataat 180
 cgaggacgcg cccgctaatt ttaataacgc tatctgcgga taaagcagaa taggtgggta 240
 accccagaca taaaccgagg aaaataatgt tattgtattt cataatctat tgttccttag 300
 cgacagattg ctgtctgctg gttcagtaag gtaccaggag aa 342

<210> 42
 <211> 841
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(841)
 <223> n = A,T,C or G

<400> 42
 agatttactg ccaattttccg gcagatcgga aagggttaaa ccatattgat ccataagggt 60
 acgaatcacg gctataccgc caggcatggc ttgagccatg gcattaaatt ccgcaaattc 120
 gggcgctgat tcttcccacg cggttathtt ggcacacacc agatccagca aggggttntc 180
 aggatcgttg agcagcagat gatctaccag ttncagcgcc tgggtgtatt gntccttggt 240
 ctgaataccc gnnagaaaaag gtgccacagc anttagcttn tctcctgctt gcaagatgtc 300
 tggcaatngc aatcattttt tgcacttant acgatgnaca nongtaaaga aatcgnattt 360
 ttntatgccg tcataacttt acgtatgtan cactttttgc nattcnaaaa aagaccattn 420
 gctncaacac gtaaathttta ttgnccocna catttanaac ataaatgntt aaaatthttcc 480
 ccccnncnan ttttaagntn ttanagaat ngggaattac ctgcttttna atgnactcan 540
 anttttttng naataattcc tntatcnaa ctnntttttn cccaanagnc nnccaaattn 600
 cggtttnntn nttnncnngg cnttttttta cccnanaann tttattcaan nccttttttg 660
 tagntathtt naagnggntt ttnttnnatt aactttccnn ttggncaaat tttggcnat 720
 ttttatatan aattntctta tntcntaatt tnggnanccc cngatgnaan tttatggngg 780
 gantcccnnt ccctntttta tnnatgntct gggntathtt taaancctnn attaannnan 840
 c 841

<210> 43
 <211> 215
 <212> DNA
 <213> E. Coli

<400> 43
 aataactttt cgttaggcag ttttgggtgt gagggtgcaag aggggagact actgaataac 60
 tcaagtttta taatcgaggg gaaaatgggtg atggcggttca tagcaaaaacg ccctcaacca 120
 taaaggtcga gggcgcttaa gatgttaaaa acccgctatc cggttaaaaaa caatgttcaa 180
 ctaaggtcag tgacattgcy ctaaaaaaagc gaatt 215

<210> 44
 <211> 395
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(395)
 <223> n = A,T,C or G

<400> 44
 gcattattca tgagaaatgt gtatcgtaaa tcaactgaaa ttaacgcaac catttggtat 60
 ttaagggttta attatctgtg tgtgatattt tattgaatgt tttaaatatt gtttttattg 120
 gcattgctat aatattgggt atcatttgct gaatggattc agtcctaatg agtggggttt 180
 taaggggacag gcatagagta atgatacgta tgcataacca acatctttac tcattatgtc 240
 attgaatgtt gaccctatgt gtttatgaag gagaggattt ttcagttgat ctggattgnt 300
 aaattcatat aatgcgcctt tgctcatgaa tggatgccag tatgtagtgg gaaattataa 360
 atattgaaat agtccaacta cttctttatt accaa 395

<210> 45
 <211> 883
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(883)
 <223> n = A,T,C or G

<400> 45
 ataatcaggt aagaaaaggt ggcgggagat taccgtgtgt tgcgatatat tttttagttt 60
 cgcgtggcaa tacatcagtg gcaataaaac gacatatcca gaaaaatata cactaagtga 120
 atgatatctt ccgatttatc ttaatcggtt atggataacg gcaaagggtc tcgttttttc 180
 ctatacttat tcagcactca caaataaagg aacgccaatg aaaattatac tctgggctgt 240
 attgattatt ttcctgattg ggctactggt ggtgactggc gtattttaaga tgatatttta 300
 aaattaatta atgtcatcag gtccgaaaat aacgagaata tttcagtctc tcacacctgt 360
 gcgctcctgt catgtgcatt gcttcatata atcactggcg caaggagcgc cgcaggcgna 420
 gnntgcncgn cgnccacact naccccatgc cgaacttcag aantgaaaac nccntaacnc 480
 cgatngtcgg cggnggcctc cccatgcnan agtangggaa ntgccangcg ncnattaaa 540
 cgaaaggctn attncaaaga ctgggccttn cntttatctg atgtttgtcg gagaacgctc 600
 tcttgagnan gacaaatncc gccgggagcg gatttgaacn ttgcgaagca accgncccna 660
 agggngnngt cntgacnccc nncctctant nnngccttc ttttgcttna angncctcct 720
 ancngatggc ctttttngcc ntctacaaa cnntttggtt aatgcttnta aaancctttc 780
 canntncaa tccngtnntn cccatccnnn tnntgaaagn ntncctnccn tgtncantnt 840
 anntnngggg gnnngnggcc ggcggncccc ccccccccc ccc 883

<210> 46
 <211> 1024
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(1024)
 <223> n = A,T,C or G

<400> 46
 gtttatggat aacggcaaag ggcttcgttt tttcctatac ttattcagca ctcacaaata 60
 aaggaacgcc aatgaaaatt atactctggg ctgtattgat tattttcctg attgggctac 120
 tgggtggtgac tggcgatatt aagatgatat tttaaaatta attaatgtca tcagggtccga 180
 aaataacgag aatatttcag tctctcatcc tgttgcgctc ctgtcatgtg cattgcttca 240
 tataatcact ggcgcaagga gcgcgcagag tncctcnant nnnntnntt ntntnnctnn 300

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nccttcaena tncnnccnncn nantnnatag nncaccnntn ttnntcnncnn gncncctcc 360
nnncnnnnnnn ncatnnnatc ccactnnntt tntccannn nnnnnnnntn canccnacaa 420
antncnaccn anntnacctt atacnnannc nannnnnnnn nncactctn nctcgnnctc 480
cccnttcnac nncannnnnn cancnntcnn ctnnnnccct nncntaatn ttctnnctan 540
ntcctancn cnncannncc cancnatccn nnnatacant cnattnnntn cnntcnctn 600
cnccnnttcc nncnnnnncn tncncatnc ccnnnnannan canntncccc ncctnccctna 660
ccnncnncncc ccccatccc nnnccnncnt ccnnantnga caannnnaat cncnnnnncn 720
nnnnnnnnnn tnnnncccn gcnncnccnt nccntcacnc tnnnnnncta nannnnntac 780
nntnacnnt cctnncaenc tncctnnng antcncacna ntnnnnnanc nanaacnctn 840
tnnnnccata atcccacacc acnccctnc ancntntnt ncntctccc ttctatcnc 900
agctnnnnnt nctntnnnnc tncncccn cnnactncnn nnaccnncn cccantcagt 960
ccacnctcn cnnnnnnntn nnnnnannan ctnncaenc cnantaacct nntnncacct 1020
tccc 1024

```

<210> 47
 <211> 236
 <212> DNA
 <213> E. Coli

```

<400> 47
atatacacta agtgaatgat atcttccgat ttatcttaat cgtttatgga taacggcaaa 60
gggcttcgtt ttttccata cttattcagc actcacaat aaaggaacgc caatgaaaat 120
tatactctgg gctgtattga ttattttcct gattgggcta ctgggtggtga ctggcgatt 180
taagatgata ttttaaaatt aattaatgtc atcaggtccg aaaataacga gaatat 236

```

<210> 48
 <211> 418
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(418)
 <223> n = A,T,C or G

```

<400> 48
cggagattac cgtgtgttgc gatataTTTT ttagtttgcg gtggcaatac atcagtggca 60
ataaaacgac atatccagaa aaatatacac taagtgaatg atatcttccg attnatctta 120
ntcgtttatg gataacggca aagggttcg ttttttcta tacttattca gactcacia 180
ataaaggaac gccaatgaaa attatactct gggctgtatt gattattttc ctgattgggc 240
tactgggtgt gactggcgta ttttaagatga ttttttaaaa ttaattaatg tcatcaggtc 300
cgaaaataac gagaatattt cagtctctca tcctgttgcg ctccgtgcat gtgcattgct 360
tcatataatc actggcgcaa ggagcgcgca nggggcggcc aatcgccgcc ggccctg 418

```

<210> 49
 <211> 550
 <212> DNA
 <213> E. Coli

```

<400> 49
ctgctagtta cagggaacac taatgacaga cagctaaaag cctgttttaa ttacgtatta 60
caaacagggg atgccagcg ttttcgtgca tttattggtg agatagcgga acgcgcacca 120
caagaaaagg agaaactgat gaccattgct gacagattac gtgaagaagg cgcaatgcag 180
ggcaaacacg aagaagccct gcgtattgct caggagatgc tggatagagg tttagacaga 240
gagttagtta tgatggtgac ccgactttca ccagacgatc ttatcgcgca aagccactaa 300
tcctgtaaca ccgggagtta actggcggat gtttgcgtga aaccacatca gcgaacgaca 360
tccgccagcg cctcttctaa atcgtaccag cgaaacgcaa aaccgcgttc ttccagccgt 420

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ttaggcagcg	cgcgttgctc	acctaatacc	agtactgaag	attcgcccat	taacagtcga	480
atggcggctc	cggggacgcg	caaaatggcc	gggcgatgca	gcgcgatgacc	gagcgcgatgg	540
gcaaattgtt						550

<210> 50
 <211> 99
 <212> DNA
 <213> E. Coli

<400> 50		
ttggcatctc	ggtgttgccg	atcttcatga
cggttttgc	gttatccatt	gagtcacgga
		actgcccct
		60
		99

<210> 51
 <211> 259
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(259)
 <223> n = A,T,C or G

<400> 51						
ccgtgccgag	atgatcctgt	naccatcatc	cgttgtgaag	tagtgattca	cgacttcaag	60
gcgcttttca	aaagggtatt	ttggctttga	catattaggg	gctattccat	ttcatcgnc	120
aacaaaatgg	gtgcagtaca	tactcnttgg	aaatcaacac	aggaggctgg	gaatgccgca	180
gaaatataga	ttactttctt	taatagtgat	ntgtttcacg	cttttatttt	tnaaanaagt	240
tnggcttact	tcccggggn					259

<210> 52
 <211> 877
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(877)
 <223> n = A,T,C or G

<400> 52						
cagcagagcg	cggccttctt	cgtcagattt	cgcagtagtg	gtaatggtaa	tatccaaacc	60
acgaacgcgg	tcgactttat	cgtagtcgat	ttctgggaag	atgatctgct	cacggacacc	120
catgctgtag	ttaccacgac	cgtcgaaaga	cttagcggac	aggccacgga	agtcacggat	180
acgaggtaca	gcaatagtga	tcaggcgctc	aaagaactcc	cacatgcgtt	cgccacgcag	240
agttacttta	cagccgatcg	gatagccctg	acggattttg	aagcctgcaa	cagatttgcg	300
tgctttgggtg	atcagcggtt	tttgaccgga	gattgctgcc	aggtctgctg	ctgcgttatc	360
cagcagtttt	ttgtcagcga	tcgcttcacc	aacacccatg	ttcagggtga	tcttctcgac	420
ccgagggact	tgcatgacag	aattgtagtt	aaactcagtc	atgagttttt	taactacttc	480
gtctttgtag	taatcatgca	gtttcgccat	cgtactactc	catgtcgggtg	aacgctctcc	540
tgagtaggac	aaatccgccc	ggagcggatt	tgaacgttgc	gaagcaacgg	cccggagggt	600
ggcgggcagg	acgcccgcga	taaaactgcca	ggcatcaa	taagcagaag	gccatcctga	660
cggatggcct	ttttgcgttt	ctacaaaactc	ttttgggttat	ttttctaaat	cattcaaata	720
tgtatccgnt	catcccatcc	tatcgatgat	aagctgtcaa	acatgagaat	ttaatcaatc	780
taaagtttta	tggngttaaa	cttgggctgg	cagnttncca	atggctta	cagtngaggg	840
ccctatntta	acgaactngg	ctantttngg	tcaatcn			877

<210> 53
 <211> 291
 <212> DNA
 <213> E. Coli

<400> 53
 tgaacagcag agatacggcc agtgcggcc atgttttttg tcctttaaac ataacagagt 60
 cctttaagga tatagaatag gggatatagct acgccagaat atcgtatttg attattgcta 120
 gtttttagtt ttgcttaaaa atattgttag ttttattaaa tgcaaaacta aattattggg 180
 atcatgaatt tgttgatga tgaataaaat ataggggggt atagatagac gtcattttca 240
 taggggtata aatgcgacta ccatgaagtt ttttaattgaa agtattgggt t 291

<210> 54
 <211> 282
 <212> DNA
 <213> E. Coli

<400> 54
 ttattaaatg caaaactaaa ttattggtat catgaatttg ttgtatgatg aataaaatat 60
 aggggggtat agatagacgt cattttcata gggttataaa tgcgactacc atgaagtttt 120
 taattgaaag tattgggttg ctgataattt gagctgttct attcttttta aatatctata 180
 taggtctgtt aatggatttt atttttacaa ttttttgtgt ttaggcataa aaaaatcaac 240
 ccgccatatg aacggcggtg taaaatatat acaacttagc aa 282

<210> 55
 <211> 293
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(293)
 <223> n = A,T,C or G

<400> 55
 cggggtccgg cgctcatcaa caatcggggg gcagcaaggg gctgaaacgg gaaagcccct 60
 cccgaagaag gggccttgta taaggaaagg gttatgatga agctcgatcat catactgggt 120
 gtgtngttac tgttaagttt cccgacttac taacaactca tcagaggggg gagaaatcct 180
 cccttaccct tgttccttta ctctagggtg aaaaaacaac agcgtcaata ggcctgccat 240
 gtacgaagcg agatctgtga accgctttcc ggtagcctt ttttatcctg ttg 293

<210> 56
 <211> 300
 <212> DNA
 <213> E. Coli

<400> 56
 tctgcgttcc gctaaaagggt gcaaatgctc aggacgttgc agcgttttgc gtgaccgctc 60
 ggggaaggca aaattgcctc tgggaaagca ttgcgcgggg tccggcgctc atcaacaatc 120
 ggggggcagc aaggggctga aacgggaaag cccctcccgga agaaggggcc ttgtataagg 180
 aaagggttat gatgaagctc gtcatcatatc tgggttgtgt gttactgtta agtttccgga 240
 cttactaaca actcatcaga ggggggagaa atcctccctt acccttgctc ctttactcta 300

<210> 57
 <211> 359
 <212> DNA
 <213> E. Coli

```

<400> 57
caacacagga ggctgggaat gccgcagaaa tatagattac tttctttaat agtgatttgt      60
ttcacgcttt tttttttcac ctggatgata agagattcac tgtgtgaatt gcatattaaa      120
caggagagtt atgagctggc ggcgttttta gcctgcaaat tgaaagagta agagtcttcg      180
gggggaaatt attcccgcct tacttacggc gttgcgcatt ctcatcgac ccaaatttat      240
tcttcacaaa aataataata gattttatta cgcgatcgat tttttatttc ctgaaaacaa      300
ataaaaaaat ccccgccaaa tggcagggat cttagattct gtgcttttaa gcagagatt      359

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```

<210> 58
<211> 700
<212> DNA
<213> E. Coli

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<220>
<221> misc_feature
<222> (1)...(700)
<223> n = A,T,C or G

```

```

<400> 58
aaacottttt ctctgtttt tcatagaggg caacccatgt cctgacctgg gttcggggga      60
caccaaaacg tgccgagatg atcctgtaac catcatcagt tgtgaagtag tgattcacga      120
cttcaaggcg cttttcaaaa gggatatttg gctttgacat attaggggct attccatttc      180
atcgtccaac aaaatgggtg cagtacatac tcgttggaat tcaacacagg aggctgggaa      240
tgccgcagaa atatagatta ctttctttta tagtgatttg tttcacgctt ttatttttca      300
cctggatgat aagagattca ctgtgtgaat tgcattataa acaggagagt tatgagctgg      360
cggcgttttt agcctgcaaa ttgaaagagt aagagtcttc ggcggggaaat tattcccgcc      420
ttacttacgg cgttgcgcac tctcattgca cccaaattta ttcttcacaa aaataataat      480
agattttatt acgcgatcga ttattttatt cctgaaaaca aataanaaaa tccccgccaa      540
atggcaggga tcttagattc tgtgctttta agcagagatt acaggctggg tacgttacca      600
gctgcggggc ctttaacgcc gctttcgatg gtgaaggaca ctttctgacc ttcgtccaga      660
gattgtaacc atcgggtctgg atagccnaga aatgtccaac      700

```

```

<210> 59
<211> 631
<212> DNA
<213> E. Coli

```

```

<220>
<221> misc_feature
<222> (1)...(631)
<223> n = A,T,C or G

```

```

<400> 59
tggtggcatt ggttgcctga gagagaaaaa ccccgcacgt tgcaggatat cacctgacaa      60
caccacgggg gctaactctt actctagacc actcaagaat agccgcgaaa cgttgtcatt      120
acaacacagg cggctatatg acgttcgcag agctgggcat ggctttcttg catgatttag      180
cggctccggc cattgtctggc attcttgcca gtatgatcgt gaactggctg aacaagcgga      240
agtaacgtgt catgcggggc tcaggctgcc gtaatggcaa tttgcgcccg gaccaggccg      300
cagggggaaa actctgcggc ctttttcggt cttactgagg gtaaggcacc cagtcgccgc      360
cgttcaggcg aacgtacggt ttatcctggt attgaataac tactgcattt gagttctcgg      420
agaccggtgc tgtttgtggc aacccactgg tgagtttttt ccagtcaaca ttgtcttcgg      480
tgaaaatctt gccatcgaga acgcgaacca ccagatcgga gatagccagg aagctgctcg      540
gttggttcgat gacaatcggg gccccctgat gcggtgcctt catgccgaag aatttcaccc      600
caacggggac gtcngtgata gaccgggcta g      631

```

```

<210> 60

```

<211> 648
 <212> DNA
 <213> E. Coli

 <220>
 <221> misc_feature
 <222> (1)...(648)
 <223> n = A,T,C or G

```

<400> 60
ggctcaggcn tgctgattgt ttttttgtgc aatggcccng tattagcgtc gttgctgtcg      60
atggagagaa tcataaacgt ggtgaatgat gattgttagc aaggaaaact gtcaaaaatc      120
ttcaaaaaat ttgagggata aggccggaat ggctccggcc agaggggaagt taaccgcgaa      180
gctgttgctg cttgagggtc gttttaacca gacgccaggc gctccatacg ccaaaccgc      240
gtctggccca gcggaccagc atattaggat ggcgaatcgt ccagatcgcc atcacgctac      300
tgccaaccag cgcccaggag cgcagactta gcagcatatt ccancgacga tcgtaagcgc      360
ctgttgcttc cagccattca cgacgactgg cggaagggnc cgcgncgtgac caacttgnc      420
tttagnctga tncanattan attnataaac gcagnanncn ggtntgatta atcntatttn      480
gctctngtct ggtagttagc nncggnnngt ctcntntna cccnnttcnn tttannttac      540
natnngtaan ttatntttnt nngtctnant tntanttgng tactntaagt ntatncgnnn      600
atnntnnnan nnnncagnnc ntntttttta aatnntttnt nanncnnc      648
  
```

<210> 61
 <211> 737
 <212> DNA
 <213> E. Coli

 <220>
 <221> misc_feature
 <222> (1)...(737)
 <223> n = A,T,C or G

```

<400> 61
tgctaataatc tttctcattg agatgaaaat taaggtaagc gaggaaacac accacaccat      60
aaacggaggc aaataatgct gggtaatatg aatgttttta tggccgtact gggaataatt      120
ttattttctg gttttctggc cgcgtatttc agccacaaat gggatgacta atgaacggag      180
ataatccctc acctaacggc ccccttgcta cagttgtgta caaggggcct gatttttatg      240
acggcgaaaa aaaaccgcca gtaaacgggc ggtgaatgct tgcattggata gatttgtgtt      300
ttgcttttac gctaacaggc attttcctgc actgataacg aatcgttgac acagtagcat      360
cagttttctc aatgaatgtt aaacggagct taaactcggc taatcacatt ttgttcgtca      420
ataaacatgc agcgatttct tccggtttgc ttacctcat acattgcccg gtccgctctt      480
ccaatgacca catccagagg ctcttcagga aatgcgcgac tcacacctgc tgtcacggta      540
atgttgatat gcccttcaga atgtgtgatg gcattggtat cgactaactg gcaaattctg      600
acacctgcac gacatgcttc ttcattcata gccgctttga caataatgat aaattcttcg      660
ccccgtagc gataaacggt ttcgtaatna cgcgtccaac tgggntaagt aaagttgcca      720
gggtgccgta atcttac      737
  
```

<210> 62
 <211> 648
 <212> DNA
 <213> E. Coli

 <220>
 <221> misc_feature
 <222> (1)...(648)
 <223> n = A,T,C or G

```

<400> 62
tgcttttgaa tatgtgctcg caatcttgag aaggaaatgg cgaccacgaa agaaaaggca      60
aaaaccgata atctgaaaga acccaagtat ttcagtataa gcattgaatg ccgaccagta      120
aactctttcg gattcaccca gaaagtgaan ccaaaatgat aatcgtatac ataagtcttt      180
cgagtggctc gtttagcaaaa agtttcaaca atggagtaaa tacatccaac atatcaataa      240
ctctcaactg taaggggatt gaaatggtaa cccagctct tcgcttgagg ggtatagccg      300
agaccaccga agccccggag gtgggtgaaat aaaaccgggc acaacacgaa agggcgcatt      360
tccgatatac ataaaagaag tcgggtcttt gtctggtaaa attaaattgg tgggaagtgc      420
gcctccgggt tgtaaatacc gactttgctg ggtgtagcct ggcgcatca agtttttttc      480
tggaagtctg ctgatgtccg ccttttttaa agggaatttt ggtgatgccg gtgaatgccg      540
cttaaccccc cgtgggcccc gttaaaagtc atggtaagnc ctaatnggtt tggggtgagg      600
aaagccnact gnnatttggg tacctggttt gcaagtancc ctggaagg      648

```

```

<210> 63
<211> 237
<212> DNA
<213> E. Coli

```

```

<220>
<221> misc_feature
<222> (1)...(237)
<223> n = A,T,C or G

```

```

<400> 63
ggtgtttant tacaagagat tcatctttgt ntaaancccn gataagtaat tacgcataaa      60
acaacaatga ttataatagc aaaaataaat attatcatct ttgatagatt acttgagata      120
gccagcatct tgtaaaagcct ttatcgTTTT tttatgctct ggattaatat aatcactaca      180
tctatctgag caatctgttg ttgatggaca tgtcaaccca tggtcattta cagccaa      237

```

```

<210> 64
<211> 427
<212> DNA
<213> E. Coli

```

```

<400> 64
gataattaga gtttgcgtc agaaaattga cgttacccat aacaaatgaa aggccaggta      60
aatcatgcc aatgacattg ttgctatcgg tgtaatcttg ttgttgctcc tgatgatccg      120
cttcaaaatg aacggcttca tcgctctcgt cctcgtggcg cttgctgttg gattaatgca      180
aggaatgccg ctggataaag ttattggctc catcaaagcc ggtgtcggcg ggacgctcgg      240
tagccttgcc ctgatcatgg gttttggcgc aatgctgggc aaaatgctgg cagactgcgg      300
tggcgacaaa cgtatcgcca ccacgctgat tgccaaattt ggtaaaaaaac acatccagtg      360
ggcggtggtg ctgaccggtt ttaccgcttg ttttgccctg ttctatgaag tgggctttgt      420
gctgatg      427

```

```

<210> 65
<211> 261
<212> DNA
<213> E. Coli

```

```

<220>
<221> misc_feature
<222> (1)...(261)
<223> n = A,T,C or G

```

```

<400> 65
caaagaacct tcaacatgaa aaatatccat ttgtttgcaa aaaaagatta ttaggaagga      60
aattaatgca attatcgaaa attcaaaaaa tatccaaaaa tngtatactt tattccagaa      120

```


<213> E. Coli

<400> 71

tttgttggct taatattcta ttgttatctt tttttataga tgtttatatt gcatgaggtg	60
gtttttggag agaagaatga ggaagatgcg tgcagccaca gaaacgttag ctttacatat	120
agcggaggtg atgtgaattt aatttacaat agaaataatt tacatatcaa acagtttagat	180
gctttttgtc g	191

<210> 72

<211> 244

<212> DNA

<213> E. Coli

<400> 72

ggccatttat acaggaaaag cctatgtcag aacgtaaaaa ctcaaaatca cgccgtaatt	60
atctcggttaa atgttcctgc ccaaactgca cccaagagtc agaacacagt ttttcaagag	120
tacaaaaagg tgcccttttg atctgccctc attgcaacaa agtattccag acaaatctta	180
aagctgtagc ctgattgatt ttattagtaa caagtatttt ttatatatta ataatatatt	240
taaa	244

<210> 73

<211> 327

<212> DNA

<213> E. Coli

<220>

<221> misc_feature

<222> (1)...(327)

<223> n = A,T,C or G

<400> 73

aaattttcag gtaccttgtc accatacttt tttttctgag cattaatgat attttgagct	60
tcttgaggat ctttaactcc ccacatttgg tggaaagtat tcatattaaa aggaagngtg	120
aataatttgn ctttataaat cgccagtgga gaattagtaa aacgattaaa ttctactaaa	180
tnattaaccg naaaaaaatt cccatatata tttatcattg gtatgaaaaa tatgtgcacc	240
atatttatga atntggatac cctnacagtc ctctgtgtac gcatttccac cgatattgatt	300
tctttttctna atcactaaaa ctttttt	327

<210> 74

<211> 150

<212> DNA

<213> E. Coli

<400> 74

gcagtgatcg aagcgatgac gaagtgtatg gaaaaatcag aaaaactcag caaatcctga	60
tgactttcgc cggacgtcag gccgccactt cgggtcgggtt acgtccggct ttctttgctt	120
tgtaaagcgc caaatctgcc gatttcaacc	150

<210> 75

<211> 330

<212> DNA

<213> E. Coli

<400> 75

gaaagtatct tcgttattga catcactgga aaatataact tgcttttcat tattaaactc	60
gaagcgcgta ccgtatctgg acaaacattt atcgagctta ccaaattcct gaagaggttt	120
aactacagat aacatttgcg cgtcctttgc agtaatgcc gtcaaactcct tgacgggcat	180

tatttagatt aaattaccag tatttcttcg	gagtgaagaa tattaccagg tatatttaac	240
acccacgttc gcgagaccag cttgatctac	gtcaccacca ccgaggtagt tagcatcggt	300
ataggcgctg aagttcttgg tgaagctaaa		330

<210> 76
 <211> 194
 <212> DNA
 <213> E. Coli

<400> 76		
tggttttttc cagcaacgga gcaaaagggt	tgcccttgtg cagctcaggg ttaaccactt	60
taactacgtg gcgacgaccc ggagatgtcg	gtttacattt acaactgcc attgtattac	120
tcttcgact tactcagcgc cgccaacgaa	gtccagattc tggccttctt tcaggggtgac	180
gtaagctttt ttcc		194

<210> 77
 <211> 188
 <212> DNA
 <213> E. Coli

<400> 77		
tccctttaac taccaggggtg ttaacgactt	cgacttcgac ttcaaacagt ttctgcacag	60
cagctttgat ttctgctttg gtcgcgtctt	tagcaacttt gagtactatg gtgttggatt	120
tttccatcgc agtagacgct ttttcagaaa	cgtgcgggtgc acgcagcacc ttcagcagac	180
gttctttca		188

<210> 78
 <211> 173
 <212> DNA
 <213> E. Coli

<400> 78		
acaaaggcga acaaagcctg tgaagcccga	aggctccaca gacagtgccta cttgaaggcc	60
ttactgtttc ttcttaggag cgagcaacct	gatcatctgg cggccttcga tcttggttgg	120
gaaggattcg accactgccg gttctttgcaa	atcgtctttc acgcgattaa gca	173

<210> 79
 <211> 272
 <212> DNA
 <213> E. Coli

<220>
 <221> misc_feature
 <222> (1)...(272)
 <223> n = A,T,C or G

<400> 79		
tggagaaaac gggtgattga taaagcaatc	atcgttctag gggcgttaat tgcgctgctg	60
gaactgatcc cgctttctgc ttcaagcttc	tgaactggat acggaaacgt aatnagggct	120
aaagaagaca ctactcttag ccctttaaca	tttaacgcat tgtcacgaac tcttctgccg	180
ccgttggtg aatggcgacg ggtattggtc	gaaatctttt ttgggtggcc ccatctttaa	240
cgcccacccg cgaaaaccctg caacatttgc	tc	272

<210> 80
 <211> 259
 <212> DNA
 <213> E. Coli

<210> 86
 <211> 1185
 <212> DNA
 <213> E. Coli

<400> 86

gtgtctaaaag	aaaaatttga	acgtacaaaa	cgcacggtta	acgttggtac	tatcggccac	60
gttgaccacg	gtaaaactac	tctgaccgct	gcaatcacca	ccgtactggc	taaaacctac	120
ggcggtgctg	ctcgtgcatt	cgaccagatc	gataacgcgc	cggaagaaaa	agctcgtggt	180
atcaccatca	acactttctca	cgttgaatac	gacaccccga	cccgtcacta	cgcacacgta	240
gactgcccgg	ggcaacgcga	ctatgtttaa	aacatgatca	ccggtgctgc	tcagatggac	300
ggcgcgatcc	tggtagttgc	tgcgactgac	ggcccgatgc	cgcagactcg	tgagcacatc	360
ctgctgggtc	gtcaggtagg	cgttccgtac	atcatcgtgt	tcctgaacaa	atgcgacatg	420
gttgatgacg	aagagctgct	ggaactgggt	gaaatggaag	ttcgtgaact	tctgtctcag	480
tacgacttcc	cgggcgacga	cactccgata	gttcgtgggt	ctgctctgaa	agcgtcggaa	540
ggcgacgcag	agtgggaagc	gaaaatcctg	gaactggctg	gcttcctgga	ttcttatatt	600
ccggaaccag	agcgtgcgat	tgacaagcgc	ttcctgctgc	cgatcgaaga	cgtattctcc	660
atctccggct	gtggtaccgt	tgttaccggg	cgtgtagaac	gcggtatcat	caaagttggt	720
gaagaagttg	aaatcgttgg	tatcaaagag	actcagaagt	ctacctgtac	tggcgttgaa	780
atgttccgca	aactgctgga	cgaaggccgt	gctgggtgaga	acgtagggtg	tctgctgcgt	840
ggtatcaaac	gtgaagaaat	cgaacgtggg	caggtagctg	ctaagccggg	caccatcaag	900
ccgcacacca	agttcgaatc	tgaagtgtac	attctgtcca	aagatgaagg	cggccgtcat	960
actccgttct	tcaaaggcta	ccgtccgcag	ttctacttcc	gtactactga	cgtgactggg	1020
accatcgaac	tgcccggaag	cgtagagatg	gtaatgccgg	gcgacaacat	caaaatgggt	1080
gttaccctga	tccacccgat	cgcgatggac	gacgggtctg	gtttcgcaat	ccgtgaaggc	1140
ggccgtaccg	ttggcgcggg	cgttgttgc	aaagttctgg	gctaa		1185

<210> 87
 <211> 2115
 <212> DNA
 <213> E. Coli

<400> 87

atggctcgta	caacacccat	cgcacgctac	cgtaacatcg	gtatcagtgc	gcacatcgac	60
gccggtaaaa	ccactactac	cgaacgtatt	ctgttctaca	ccggtgtaaa	ccataaaatc	120
ggtgaagttc	atgacggcgc	tgcaaccatg	gactggatgg	agcaggagca	ggaacgtggt	180
attaccatca	cttccgctgc	gactactgca	ttctgggtctg	gtatggctaa	gcagtatgag	240
ccgcacgcga	tcaacatcat	cgcacccccg	gggcacgttg	acttcacaat	cgaagtagaa	300
cgttccatgc	gtgttctcga	tgggtgcggta	atggtttact	gcgcagttgg	tgggtgttcag	360
ccgcagctctg	aaaccgtatg	gcgtcaggca	aacaaatata	aagttccgcg	cattgcgttc	420
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cgtctgggcg	cgaacccggg	tccgctgcag	ctggcgattg	gtgctgaaga	acatttcacc	540
ggtgttggtg	acctggtgaa	aatgaaagct	atcaactgga	acgacgctga	ccaggggcgta	600
accttcgaat	acgaagatat	cccggcagac	atggttgaa	tggttaacga	atggcaccag	660
aacctgatcg	aatccgcagc	tgaagcttct	gaagagctga	tggaataata	cctgggtggt	720
gaagaactga	ctgaagcaga	aatcaaagg	gctctgcgtc	agcgcgttct	gaacaacgaa	780
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gcggtaattg	attacctgcc	atccccgggt	gacgtacctg	cgatcaacgg	tatcctggac	900
gacggtaaag	acactccggc	tgaacgtcac	gcaagtgatg	acgagccgtt	ctctgcactg	960
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ggtcgtatcg	ttcagatgca	cgctaacaaa	cgtgaagaga	tcaaagaagt	tcgcgcgggc	1140
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gaaccgaaaa	ccaaagctga	ccaggaaaaa	atgggtctgg	ctctgggccg	tctggctaaa	1320
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atgggcgaac	tgcacctcga	catcatcggt	gaccgtatga	agcgtgaatt	caacggtgaa	1440
gcgaacgtag	gtaaaccgca	ggttgcttac	cgtgaaacta	tccgccagaa	agttaccgat	1500
gttgaaggta	aacacgcgaa	acagtctggt	ggtcgtggtc	agtatgggtca	tgttggttatc	1560
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tttaaagaag	gctttaagaa	agcgaaacca	gttctgcttg	agccgatcat	gaaggttgaa	1860
gtagaaactc	cggaagagaa	caccggtgac	gttatcggtg	acttgagccg	tctgctggtg	1920
atgctcaaa	gtcaggaatc	tgaagttact	ggcggttaaga	tccacgctga	agtaccgctg	1980
tctgaaatgt	tccgatacgc	aactcagctg	cgttctctga	ccaaaggctg	tgcatacatc	2040
actatggaat	tccgtaagta	tgatgaagcg	cggagtaacg	ttgctcaggc	cgtaatgaa	2100
gcccgtggtg	aataa					2115

<210> 88
 <211> 540
 <212> DNA
 <213> E. Coli

<400> 88						
atgccacgtc	gtcgcgtcat	tggtcagcgt	aaaattctgc	cggatccgaa	gttcggatca	60
gaactgctgg	ctaaatttgt	aaatatcctg	atggtagatg	gtaaaaaatc	tactgctgaa	120
tctatcgtag	acagcgcgct	ggagaccctg	gctcagcgtc	ctggtaaatac	tgaactggaa	180
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gcgaacgaac	tttctgatgc	tgcagaaaaac	aaagggtactg	cagttaagaa	acgtgaagac	420
gttcaccgta	tggccgaagc	caacaaggcg	ttcgcacact	accgttggtt	atcccttcgg	480
agtttttagtc	accaggcggg	cgttccagtc	aagcagcccg	ctttgggcta	cttaaattga	540

<210> 89
 <211> 1549
 <212> DNA
 <213> E. Coli

<400> 89						
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tgtctgggaa	gctgcctgat	ggagggggat	aactactgga	aacggtagct	aataccgcat	180
aatgtcgcaa	gaocaaagag	ggggaccttc	gggcctcttg	ccatcggtatg	tgcccagatg	240
ggattagctt	gttgggtggg	taacggctca	ccaaggcgac	gatccctagc	tggtctgaga	300
ggatgaccag	ccacactgga	actgagacac	ggtccagact	cctacgggag	gcagcagtg	360
ggaatattgc	acaatgggag	caagcctgat	gcagccatgc	cgcgtgtatg	aagaaggcct	420
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agatgtgaaa	tcccggggct	caacctggga	actgcacttg	atactggcaa	gcttgagtc	660
cgtagagggg	ggtagaattc	caggtgtagc	ggtagaatgc	gtagagatct	ggaggaatac	720
cgggtggcgaa	ggcgggcccc	tggacgaaga	ctgacgtcca	ggtgcgaaag	cgtggggagc	780
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aagggttaaaa	ctcaaatgaa	ttgacggggg	ccgcacaag	cggtagagca	tgtgggttaa	960
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gaatgtgcct	tccgggaaccg	tgagacaggt	gctgcatggc	tgtcgtcagc	tctgtgtgtg	1080
aaatgttggg	ttaagtcccg	caacgagcgc	aaccttatc	ctttgttgcc	agcggtcocg	1140
cggggaactc	aaaggagact	gccagtgata	aactggagga	aggtggggat	gacgtcaagt	1200
catcatggcc	cttacgacca	gggctacaca	cgtgctacaa	tggcgcatac	aaagagaagc	1260

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 <213> E. Coli

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 <213> E. Coli

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 <212> DNA
 <213> E. Coli

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<210> 95
 <211> 1227
 <212> DNA
 <213> E. Coli

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 <213> E. Coli

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<210> 97

<211> 771

<212> DNA

<213> E. Coli

<400> 97

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<211> 1335

<212> DNA

<213> E. Coli

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1335

<210> 99
<211> 1536
<212> DNA
<213> E. Coli

<400> 99

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<211> 1029
<212> DNA
<213> E. Coli

<400> 100

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<400> 103

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<210> 104

<211> 291

<212> DNA

<213> E. Coli

<400> 104

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<210> 105

<211> 1152

<212> DNA

<213> E. Coli

<400> 105

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<210> 106

<211> 3048
 <212> DNA
 <213> E. Coli

<400> 106

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<210> 107
<211> 885
<212> DNA
<213> E. Coli

<400> 107

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<210> 108
<211> 654
<212> DNA
<213> E. Coli

<400> 108

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tatcgtgaaa	tcgagaaggc	agaagcgaaa	aaagagagtg	aagaagggat	ataa	654

<210> 109
<211> 261
<212> DNA
<213> E. Coli

<400> 109

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tgcgtagggc	actacgagac	accaacctgc	cagaagggtg	gcccgatccc	caatactatt	180
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caccacgcgg	ataaaattta	a				261

<210> 110
<211> 1203
<212> DNA
<213> E. Coli

<400> 110

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<210> 111

<211> 1179

<212> DNA

<213> E. Coli

<400> 111

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<210> 112

<211> 1326

<212> DNA

<213> E. Coli

<400> 112

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 <212> DNA
 <213> E. Coli

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<210> 114
 <211> 363
 <212> DNA
 <213> E. Coli

<400> 114						
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tga						363

<210> 115
 <211> 921
 <212> DNA

<213> E. Coli

<400> 115

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gacggcagca	aagacgctac	ggagtcaatc	attaatgctc	tggctgtttc	agatcctcta	180
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<210> 116

<211> 1332

<212> DNA

<213> E. Coli

<400> 116

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gtaatatata	tttatttcatt	atatgcgata	tttacttcac	atataaaaaac	agaaagggtat	360
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<210> 117

<211> 249

<212> DNA

<213> E. Coli

<400> 117

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ggcagcttcg	tggttgccgt	tattggtgcg	attgtcgtgc	tatttatcta	caggaagatt	240
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<210> 118

<211> 183

<212> DNA

<213> E. Coli

<400> 118

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gatctggtga	ataccgtacg	ttcttatgac	acggaaaacg	aacatgatgt	ttgtggttgg	180
taa						183

<210> 119

<211> 360

<212> DNA

<213> E. Coli

<400> 119

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<210> 120

<211> 741

<212> DNA

<213> E. Coli

<400> 120

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<210> 121

<211> 1395

<212> DNA

<213> E. Coli

<400> 121

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<211> 3123
<212> DNA
<213> E. Coli
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Variable	Mean	SD	Min	Max
Age	34.5	10.2	18	65
Gender	0.5	0.5	0	1
Marital status	0.6	0.5	0	1
Education	12.5	1.5	9	16
Income	15.2	5.8	5	35
Health status	1.2	0.8	0	3
Stress level	2.1	1.1	1	4
Life satisfaction	3.8	1.2	1	5
Work engagement	4.2	0.9	3	5
Organizational commitment	4.5	1.0	3	5
Job satisfaction	4.1	0.8	3	5
Turnover intention	1.5	0.7	0	3
Organizational citizenship behavior	3.5	1.1	1	5
Employee well-being	3.2	1.0	1	5
Work-life balance	3.0	0.9	1	5
Job autonomy	3.8	1.2	1	5
Supervisor support	4.0	1.1	3	5
Team cohesion	4.3	0.8	3	5
Organizational culture	4.6	0.9	3	5
Employee engagement	4.4	1.0	3	5
Job design	3.9	1.1	1	5
Organizational climate	4.2	1.0	3	5
Employee turnover	1.8	0.8	0	3
Organizational performance	4.7	0.7	3	5
Employee loyalty	4.5	0.9	3	5
Job security	4.1	1.0	3	5
Organizational identity	4.8	0.8	3	5
Employee motivation	4.3	1.1	3	5
Job satisfaction	4.1	0.8	3	5
Organizational commitment	4.5	1.0	3	5
Employee well-being	3.2	1.0	1	5
Work-life balance	3.0	0.9	1	5
Job autonomy	3.8	1.2	1	5
Supervisor support	4.0	1.1	3	5
Team cohesion	4.3	0.8	3	5
Organizational culture	4.6	0.9	3	5
Employee engagement	4.4	1.0	3	5
Job design	3.9	1.1	1	5
Organizational climate	4.2	1.0	3	5
Employee turnover	1.8	0.8	0	3
Organizational performance	4.7	0.7	3	5
Employee loyalty	4.5	0.9	3	5
Job security	4.1	1.0	3	5
Organizational identity	4.8	0.8	3	5
Employee motivation	4.3	1.1	3	5

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<211> 1035
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<213> E. Coli
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<212> DNA
<213> E. Coli
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 <213> E. Coli

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<212> DNA

<213> E. Coli

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<211> 582

<212> DNA

<213> E. Coli

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<211> 579

<212> DNA

<213> E. Coli

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<210> 132

<211> 2223

<212> DNA

<213> E. Coli

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Figure 1 consists of 12 bar charts, labeled (a) through (l), each representing a different protein (A through L). Each chart plots the percentage of total protein (y-axis, 0 to 100) against protein concentration (x-axis, Control, 100, 200, 400, 800, 1600, 3200, 6400, 12800, 25600, 51200, 102400). The bars are color-coded by fraction: C (Control, white), S (Soluble, light blue), P (Pellet, dark blue), M (Membrane, light green), B (Biosphere, dark green), and A (Aqueous, light yellow). In all charts, the percentage of protein in the S fraction decreases as concentration increases, while the percentage in the P fraction increases. The percentage in the M fraction remains relatively constant. The percentage in the B and A fractions is very low and remains constant across all concentrations.

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7152

<210> 143

<211> 186

<212> DNA

<213> E. Coli

<400> 143

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gtatcattac tctatgcctg tcccttaaaa acccactcat taagactgaa tccattcagc 180
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186

<210> 144

<211> 1197

<212> DNA

<213> E. Coli

<400> 144

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<210> 145
 <211> 291
 <212> DNA
 <213> E. Coli

<400> 145						
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ccgctgttac	tgatgctggc	cgggtgtgcg	cctatgcatg	aaaccgcga	ggcgtaagc	180
cagcaaacgc	ccgctgcaca	agttgacacc	gcattaccca	cggcgctgaa	aatggttggc	240
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<210> 146
 <211> 948
 <212> DNA
 <213> E. Coli

<400> 146						
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cgtaaagaat	acgatgaagc	aacggaatta	tttcagcatg	ttcgggtggt	gaataattcc	900
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<210> 147

<211> 891
 <212> DNA
 <213> E. Coli

<400> 147

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gatttaacga	cgtttaaact	ggaacaaaac	agttttattg	atgaagacct	gcggcaatat	180
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gtggtgccgg	atgacgagat	tatgcaacac	cgcaaaatgg	cgctgttggg	gttaattcag	540
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acagggaaca	ctaattgacag	acagctaaaa	attacgtatt	acaaacaggg		660
gatgccccagc	gttttcgtgc	atattattggg	gagatagcgg	aacgcgcacc	acaagaaaag	720
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gaagaagccc	tgcgtattgc	tcaggagatg	ctggatagag	gtttagacag	agagttagtt	840
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<210> 148
 <211> 1668
 <212> DNA
 <213> E. Coli

<400> 148

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cgttggttcc	tcgaccgtat	cgcacgcac	attctggatt	accaggatga	aggtaaagtt	1560
gagttcttcg	aaggtaactt	taccgagtac	gaagagtaca	agaaacgcac	gctgggcgca	1620
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<210> 149
<211> 522
<212> DNA
<213> E. Coli

<400> 149

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acatggggtg	ccctctatga	aaaacatgga	gaaaaagggt	taattcccaa	acctaaaggc	180
gttagtgctg	atccagagtt	gcgtattaag	gtcgtgaaag	ctgtgatcga	gcagcacatg	240
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gaccgacgca	ttgaggatct	tgaaaggcaa	gttcgatttc	ttgaaacgcg	gcttatgtat	480
ctaaaaaagc	tgaaaagcctt	agctcatccc	acgaaaaagt	ga		522

<210> 150
<211> 852
<212> DNA
<213> E. Coli

<400> 150

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gcggacgtta	aaaagcgtat	tagtgagatt	tatcacgaga	atagaggccg	atacggatac	180
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agtaatatata	gcgaactgaa	ggatgctgtt	acggaatata	ttgaatacta	caacagcaga	780
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cctcgtgttt	aa					852

<210> 151
<211> 117
<212> DNA
<213> E. Coli

<400> 151

atgaaagttc	gtgcttccgt	caagaaatta	tgccgtaact	gcaaaatcgt	taagcgtgat	60
ggtgtcatcc	gtgtgatttg	cagtgccgag	ccgaagcata	aacagcgcca	aggctga	117

<210> 152
<211> 1332
<212> DNA
<213> E. Coli

<400> 152

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cgcagactgc	tgtttgttat	cggtgcgctg	attgtgttcc	gtattggctc	ttttattccg	120
atccctggta	ttgatgccgc	tgtacttgcc	aaactgcttg	agcaacagcg	aggcaccatc	180
attgagatgt	ttaacatgtt	ctctgggtgt	gctctcagcc	gtgcttctat	ctttgctctg	240

gggatcatgc	cgtatatattc	ggcgtcgatc	attatccagc	tgctgacggt	ggttcaccca	300
acgttggcag	aaattaagaa	agaaggggag	tctggtcgtc	gtaagatcag	ccagtacacc	360
cgctacggta	ctctgggtgct	ggcaatattc	cagtcgatcg	gtattgctac	cggtctgccg	420
aatatgcctg	gtatgcaagg	cctgggtgatt	aaccggggct	ttgcattcta	cttcaccgct	480
gttgtaagtc	tggtcacagg	aaccatgttc	ctgatgtggt	tgggcgaaca	gattactgaa	540
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ccagccattg	cccatactat	cgagcaagcg	cgtcaaggcg	acctgcactt	cctcgtgttg	660
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caacgcgcga	ttgtggtaaa	ctacgcgaaa	cgtcagcaag	gtcgtcgtgt	ctatgctgca	780
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ttcgggtggga	cctcaactgct	tatcgttggt	gtcgtgatta	tggactttat	ggctcaagtg	1260
caaactctga	tgatgtccag	tcagtatgag	tctgcattga	agaaggcgaa	cctgaaaggc	1320
tacggccgat	aa					1332

<210> 153
 <211> 435
 <212> DNA
 <213> E. Coli

<400> 153						
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actgttcgtg	gcctgcgtgt	tactaaaggc	gctcgtgctg	ctatcgaagc	tgctggcggt	420
aaaatcgagg	aataa					435

<210> 154
 <211> 180
 <212> DNA
 <213> E. Coli

<400> 154						
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<210> 155
 <211> 504
 <212> DNA
 <213> E. Coli

<400> 155						
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cataacgttc	tggctaaagc	ctatggttcc	accaacccga	tcaacgtggt	tcgtgcaact	420
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<210> 156
 <211> 354
 <212> DNA
 <213> E. Coli

<400> 156						
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cgcgctctgg	aaaaaggcat	caaagatgta	tcctttgacc	gttccggggt	ccaatatcat	300
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<210> 157
 <211> 534
 <212> DNA
 <213> E. Coli

<400> 157						
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atcactgctg	aatgtccgac	tcagactgaa	atcgtgctga	aaggcgcctg	taagcagggtg	420
atcggccagg	ttgcagcgga	tctgcgcgcc	taccgtcgct	ctgagcctta	taaaggcaag	480
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<210> 158
 <211> 393
 <212> DNA
 <213> E. Coli

<400> 158						
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ccaggctctgc	gcattctataa	acgtaaagat	gagctgccga	aagtatatgc	gggtctgggt	300
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<210> 159
 <211> 306
 <212> DNA
 <213> E. Coli

<400> 159						
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gcctggatgg	aacaaattga	taatgcagtc	gatgtcacgg	caggtgaagt	aaccgctaac	540
gcaacctacg	tgctggatta	taaataa				567

<210> 164
 <211> 1284
 <212> DNA
 <213> E. Coli

<400> 164						
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<210> 165
 <211> 1434
 <212> DNA
 <213> E. Coli

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<210> 166
 <211> 2841
 <212> DNA
 <213> E. Coli

<400> 166						
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<210> 167
 <211> 1302
 <212> DNA
 <213> E. Coli

<400> 167

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ctgcatcacg	ctattgcgac	cgggcaacgc	atcgaaattg	aacattttccg	taatgaggca	1260
aacaatcagg	aaccgttctg	gttgccacagc	ggaaaacggt	aa		1302

<210> 168
 <211> 213
 <212> DNA
 <213> E. Coli

<400> 168

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atcactcctg	acgatggctc	taaagatgtg	ttcgtacact	tctctgctat	ccagaacgat	120
ggttacaaat	ctctggacga	aggtcagaaa	gtgtccttca	ccatcgaaaag	cggcgctaaa	180
ggcccggcag	ctggtaacgt	aaccagcctg	taa			213

<210> 169
 <211> 1572
 <212> DNA
 <213> E. Coli

<400> 169

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cgacatatgc	cagcaggcgg	cgtctggtgg	tttaacgtcg	atcgccatga	agatgctatc	120
agtctggcga	atcaaacaat	tgcatcccag	gctgaaaccg	cacacgtcgc	ggtcattagc	180
atggacagcg	atccggcgaa	aatctttcaa	ttagatgatt	ctcaagggcc	ggaaaaaata	240

aaattat	caatgcta	tcata	ggtctata	atttgac	tgatttg	300
tggtctat	atccccata	ttacct	attcttg	gcgcaata	cgcatgg	360
aacattc	cgagcgg	tcgtcat	ttggata	tgaataa	gagcagg	420
aaccatt	cgctttt	aattaat	ggaaata	acgataa	attttcatt	480
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agcggtc	aacaaa	tatctgg	ttagttc	gcgaag	ggagatc	660
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ctcaaac	gtggttt	gaagtgg	gtgttct	atgccgt	caacatg	1140
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caatggg	tgccgct	tttaacg	agttcta	cggtcat	tgccgag	1500
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<210> 170
 <211> 189
 <212> DNA
 <213> E. Coli

<400> 170						
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aaacctc	atgttaa	ggccggg	ttacgcc	cgaaaa	cagggca	180
aaaaaat	ga					189

<210> 171
 <211> 1680
 <212> DNA
 <213> E. Coli

<400> 171						
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ctttccg	ggaactt	ttttctg	aagttcg	tggtgtg	gggatat	120
aacttcc	cgctcct	tttgggt	gccgcgt	tgctgat	ccttccg	180
tacagc	atcgctt	ccactgg	gccctgc	tcggctt	tttgtt	240
catgac	ggttgcc	cccgaaa	ataatga	aggttcg	ggtggcg	300
ttcagta	attattt	cgacctt	acacgct	ttaactg	gatgatt	360
gccattt	ttttatt	ggcctgg	ttcctgt	aatggat	cattacc	420
tttgtg	ccatact	atggctg	gtactta	tgccggg	aagttt	480
ttgtgg	ccggaca	gacgacc	gtaaca	cggtgtg	cgacgcg	540
accgttg	cgacggg	cgacccg	gtgggtg	tgcccgc	aactgc	600
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<210> 172
 <211> 384
 <212> DNA
 <213> E. Coli

<400> 172						
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<210> 173
 <211> 306
 <212> DNA
 <213> E. Coli

<400> 173						
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cgtaa						306

<210> 174
 <211> 405
 <212> DNA
 <213> E. Coli

<400> 174						
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<210> 175
 <211> 300
 <212> DNA

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<211> 891

<213> E. Coli

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<213> E. Coli

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<213> E. Coli

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<213> E. Coli

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<212> DNA

<213> E. Coli

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<211> 504

<212> DNA

<213> E. Coli

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<210> 186

<211> 276

Figure 1 consists of 12 bar charts, labeled (a) through (l), each representing a different category of expenditure or demographic factor. The y-axis for all charts is 'Percentage of Total Sample' ranging from 0 to 100. The x-axis for all charts represents age groups: 18-24, 25-34, 35-44, 45-54, 55-64, 65-74, and 75+.

- (a) Education:** Shows the percentage of the sample with different levels of education (High School, Some College, Bachelor's, Master's, Doctorate) across age groups.
- (b) Employment:** Shows the percentage of the sample in different employment statuses (Unemployed, Part-time, Full-time, Self-employed) across age groups.
- (c) Income:** Shows the percentage of the sample in different income brackets (Less than \$10,000, \$10,000-\$19,999, \$20,000-\$29,999, \$30,000-\$39,999, \$40,000-\$49,999, \$50,000-\$59,999, \$60,000-\$69,999, \$70,000-\$79,999, \$80,000-\$89,999, \$90,000-\$99,999, \$100,000+) across age groups.
- (d) Housing:** Shows the percentage of the sample in different housing types (Single-family detached, Single-family attached, Multi-family, Other) across age groups.
- (e) Transportation:** Shows the percentage of the sample in different vehicle types (No vehicle, Single vehicle, Two vehicles, Three or more vehicles) across age groups.
- (f) Health Insurance:** Shows the percentage of the sample with different types of health insurance (Medicare, Medicaid, Private, Other) across age groups.
- (g) Food:** Shows the percentage of the sample in different food consumption categories (Fast food, Restaurant, Home-cooked, Other) across age groups.
- (h) Entertainment:** Shows the percentage of the sample in different entertainment categories (TV, Radio, Music, Movies, Other) across age groups.
- (i) Travel:** Shows the percentage of the sample in different travel categories (Domestic, International, Other) across age groups.
- (j) Clothing:** Shows the percentage of the sample in different clothing categories (Clothing, Shoes, Accessories, Other) across age groups.
- (k) Personal Care:** Shows the percentage of the sample in different personal care categories (Cosmetics, Hair Care, Skincare, Other) across age groups.
- (l) Other:** Shows the percentage of the sample in other categories (Housing, Transportation, Health Insurance, Food, Entertainment, Travel, Clothing, Personal Care, Other) across age groups.

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 <212> DNA
 <213> E. Coli

<400> 190						
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<210> 191
 <211> 285
 <212> DNA
 <213> E. Coli

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<210> 192
 <211> 1977
 <212> DNA
 <213> E. Coli

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<210> 193

<211> 2634

<212> DNA

<213> E. Coli

<400> 193

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 <212> DNA
 <213> E. Coli

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<210> 195
 <211> 1140

<212> DNA
<213> E. Coli

<400> 195

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<211> 1371
<212> DNA
<213> E. Coli

<400> 196

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<210> 197
<211> 186
<212> DNA

<213> E. Coli

<400> 197

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tctgttcacc	gtgaagagat	ctaccagcgt	atccaggctg	aaaaatcca	gcagtccagt	180
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<210> 198

<211> 93

<212> DNA

<213> E. Coli

<400> 198

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<210> 199

<211> 603

<212> DNA

<213> E. Coli

<400> 199

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<210> 200

<211> 597

<212> DNA

<213> E. Coli

<400> 200

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<210> 201

<211> 549

<212> DNA

<213> E. Coli

<400> 201

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aacgttggtg	tgcagatcct	ggacagaacg	ggtgctgcgc	tgacgctgga	tgggtgcgaca	420
tttagttcag	aaacaaccct	gaataacgga	accaatacca	ttccgttcca	ggcgcggttat	480
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<210> 202

<211> 648

<212> DNA

<213> E. Coli

<400> 202

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gatgtgcttt	ccgtgggaga	ggggccaggg	atagccacca	atattggcgt	agcgttggtt	480
gatgatgaag	gaaacctcgt	accgattaat	cgctctccag	caaactggaa	acggctttat	540
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<210> 203

<211> 726

<212> DNA

<213> E. Coli

<400> 203

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gcattggtgc	ctccaatggg	cgaaagcacg	gttaaattgc	cttctgatgc	aggaagcaat	660
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<210> 204

<211> 2637

<212> DNA

<213> E. Coli

<400> 204

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ggaaaagtgc	aggtgaaatg	gggagaagag	gaaaatgctc	actgtgtcgc	caattatcaa	2580
ctgccaccag	agagtcagca	gcagttatta	accagctat	cagctgaatg	tcgttaa	2637

<210> 205

<211> 531

<212> DNA

<213> E. Coli

<400> 205

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cttgcaactg	aaaatacggg	gtcagcggct	tcgggactgg	gaatacagct	tctgaatgag	360
cagcaaaaatc	aaatacccct	taatgctcca	tcgtccgcgc	tttcgtggac	gaccctgacg	420

ccgggtaaac caaatacgtc gaatttttac gcccggttaa tggcgacaca ggtgcctgtc 480
actgcggggc atatcaatgc cacggctacc ttcactcttg aatatcagta a 531

<210> 206
<211> 504
<212> DNA
<213> E. Coli

<400> 206
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caggtcagag cattgcacgt aaatggcgga gccactcagg gaaccattca ggagtgatt 480
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<210> 207
<211> 903
<212> DNA
<213> E. Coli

<400> 207
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taa 903

<210> 208
<211> 1631
<212> DNA
<213> E. Coli

<400> 208
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tgggctgcaa tcggtgtgct gggtagcctg gtttttggcc tgctgacgta tctgacaaat 240
ctttattttca agattaaaga agacaggcgt aaggctgcga gaggagagta atccaatgac 300
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tcaccaacat	gctcggagat	attgcagcag	aagctcagct	ttatgctgaa	attgctgacg	1560
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<210> 209
 <211> 534
 <212> DNA
 <213> E. Coli

<400> 209

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<210> 210
 <211> 312
 <212> DNA
 <213> E. Coli

<400> 210

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gccatggacc	gtgttgaagg	agctgcgctg	gagttttatg	aggcagcagc	cagaaggagc	180
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<210> 211
 <211> 291
 <212> DNA
 <213> E. Coli

<400> 211

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catcgggggtg	aggatatgaa	atcaatggat	aagttaacaa	cagggtgttg	ctatggcaca	120

tcggcgggta	atgctggttt	ctgggcattg	cagttactcg	ataaagtaac	tccgtcacag	180
tgggctgcaa	tcggtgtgct	gggtagcctg	gtttttggcc	tgctgacgta	tctgacaaat	240
ctttatttca	agattaaaga	agacaggcgt	aaggctgcga	gaggagagta	a	291

<210> 212
 <211> 216
 <212> DNA
 <213> E. Coli

<400> 212						
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atttctcctg	ttgatggtag	taaagatgtg	tttgtgcatt	tttctgcgat	tcagaatgat	120
aattatcgaa	ccttatttga	aggtcaaaag	gttaccttct	ctatagagag	tggtgctaaa	180
ggtcctgcag	cagcaaatgt	catcattact	gattaa			216

<210> 213
 <211> 1017
 <212> DNA
 <213> E. Coli

<400> 213						
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gagcagattc	tgccatggca	aaacatggtg	gaagtcatcg	agccgtttta	ccccaaggct	180
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<210> 214
 <211> 474
 <212> DNA
 <213> E. Coli

<400> 214						
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ttattgaaac	aaatatgcca	gcattatgca	ggcctggact	atattagtgg	aggtgtatac	180
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gatgaagcga	aatctttaca	tgattattcc	gtaagaaaat	ttcctgtgct	ttctgatttt	420
attgtgtcat	ttatgttagg	gattaaggaa	ggtgcgaaca	agtcctgat	atga	474

<210> 215
 <211> 1119
 <212> DNA

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 <212> DNA
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 <211> 1116
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 <213> E. Coli

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 <211> 1404
 <212> DNA
 <213> E. Coli

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<211> 702
<212> DNA
<213> E. Coli

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<210> 227
<211> 333
<212> DNA
<213> E. Coli

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agccacatca ctgtggttgt gtccgatcgc tga 333

<210> 228
<211> 279
<212> DNA
<213> E. Coli

<400> 228
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cgcggccacg ctgctgataa aaaagcgaag aagaaataa 279

<210> 229
<211> 822
<212> DNA
<213> E. Coli

<400> 229
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 <211> 303
 <212> DNA
 <213> E. Coli

<400> 230						
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<210> 231
 <211> 630
 <212> DNA
 <213> E. Coli

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<210> 232
 <211> 606
 <212> DNA
 <213> E. Coli

<400> 232						
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gcatga

606

<210> 233
<211> 312
<212> DNA
<213> E. Coli

<400> 233

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<210> 234
<211> 357
<212> DNA
<213> E. Coli

<400> 234

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<210> 235
<211> 198
<212> DNA
<213> E. Coli

<400> 235

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tgcttgcctg	acgcataa					198

<210> 236
<211> 543
<212> DNA
<213> E. Coli

<400> 236

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<210> 237

<211> 1929
<212> DNA
<213> E. Coli

<400> 237

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gtggaatcag	gcaaagttgc	cgttcgcacc	cgccgtggta	aagacctggg	aagcatggac	1860
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gaggaataa						1929

<210> 238
<211> 1353
<212> DNA
<213> E. Coli

<400> 238

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acctgcgtaa	atgttggctg	tgtgccgaaa	aaagtgatgt	ggcacgcggc	gcaaattccgt	180
gaagcgatcc	atatgtacgg	cccgattat	ggttttgata	ccactatcaa	taaattcaac	240
tgggaaacgt	tgatcgccag	ccgtaccgcc	tatatcgacc	gtattcatat	ttcctatgaa	300
aacgtgctcg	gtaaaaataa	cgttgatgta	atcaaaggct	ttgcccgcgt	cgttgatgcc	360
aaaacgcgtg	aggtaaacgg	cgaaccatc	acggccgatc	atattctgat	cgccacaggc	420
ggtcgtccga	gccacccgga	tattccgggc	gtggaatacg	gtattgattc	tgatggcttc	480
ttcgcccttc	ctgctttgcc	agagcgcgtg	gcggttggtg	gcgcgggtta	catcgccggt	540
gagctggcgg	gcgtgattaa	cggcctcggc	gcgaaaacgc	atctgtttgt	gcgtaaacat	600
gcgcgcgtgc	gcagcttcga	cccgatgatt	tccgaaaacg	tggtcgaaat	gatgaacgcc	660
gaaggcccg	agctgcacac	caacgccatc	ccgaaagcgg	tagtgaaaaa	taccgatggg	720

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gtggcgctga	agatgggggc	aacaaaaaaa	gacttcgaca	ataccgtcgc	cattcaccca	1320
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<210> 239
 <211> 2904
 <212> DNA
 <213> E. Coli

<400> 239						
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cccggcctat	caacgtcgtc	gtcttcaacg	ttccttcagg	acccttaaag	ggtcagggag	120
aactcatctc	ggggcaagtt	tcgtgcttag	atgctttcag	cacttatctc	ttccgcattt	180
agctaccggg	cagtgccatt	ggcatgacaa	cccgaacacc	agtgatgcgt	ccactccggt	240
cctctcgtac	taggagcagc	ccccctcagt	tctccagcgc	ccacggcaga	tagggaccga	300
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ccttggggacc	tacttcagcc	ccaggatgtg	atgagccgac	atcgaggtgc	caaacaccgc	420
cgctgatatg	aactcctggg	cggtatcagc	ctgttatccc	cggagtacct	tttatccgtt	480
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gcgccgtcac	gctcgcagtc	aagctggctt	atgccattgc	actaacctcc	tgatgtccga	600
ccaggattag	ccaaccttcg	tgctcctcgc	ttactcttta	ggaggagacc	gccccagtca	660
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ttaaagggtg	gtatttcaag	gtcggctcca	tgcagactgg	cgtccacact	tcaaagcctc	780
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ccgtatacgt	ccactttcgt	gtttgcacag	tgctgtgttt	ttaataaaca	gttgcagcca	1140
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ttaccgacgc	ttatcgcaga	ttagcacgtc	cttcacgcgc	tctgactgcc	agggcatcca	2880
ccgtgtacgc	ttagtgcgtt	aacc				2904

<210> 240
 <211> 120
 <212> DNA
 <213> E. Coli

<400> 240						
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gtttcacttc	tgagttcggc	atgggggtcag	gtgggaccac	cgcgctacgg	ccgccaggca	120

<210> 241
 <211> 76
 <212> DNA
 <213> E. Coli

<400> 241						
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cccctagggg	acgcc					76

<210> 242
 <211> 1549
 <212> DNA
 <213> E. Coli

<400> 242						
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tgtctgggaa	gctgcctgat	ggagggggat	aactactgga	aacggtagct	aataccgcat	180
aatgtcgcaa	gaccaaaagag	ggggaccttc	gggcctcttg	ccatcggatg	tgcccagatg	240
ggattagctt	gttgggtggg	taacggctca	ccaaggcgac	gatccctagc	tggtctgaga	300
ggatgaccag	ccacactgga	actgagacac	ggtccagact	cctacgggag	gcagcagtg	360
ggaatattgc	acaatggg	caagcctgat	gcagccatgc	cgctgtatg	aagaaggcct	420
tcgggttgta	aagtactttc	agcggggagg	aaggaggtaa	agttaatacc	tttgctcatt	480
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catcatggcc	cttacgacca	gggctacaca	cgtgctacaa	tggcgcatat	aaagagaagc	1260
gacctcgca	gagcaagcgg	acctcataaa	gtgcgtcgta	gtccggattg	gagtctgcaa	1320

ctcgactcca	tgaagtcgga	atcgctagta	atcgtggatc	agaatgccac	ggtgaatacg	1380
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tagcttaacc	ttcggggagg	cgcttaccac	tttgtgattc	atgactgggg	tgaagtcgta	1500
acaaggtaac	cgtaggggaa	cctgogggtg	gatcacctcc	ttaccttaa		1549

<210> 243
 <211> 221
 <212> PRT
 <213> E. Coli

<400> 243

Met	Asn	Val	Phe	Ser	Gln	Thr	Gln	Arg	Tyr	Lys	Ala	Leu	Phe	Trp	Leu
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Ser	Leu	Phe	His	Leu	Leu	Val	Ile	Thr	Ser	Ser	Asn	Tyr	Leu	Val	Gln
			20					25					30		
Leu	Pro	Val	Ser	Ile	Leu	Gly	Phe	His	Thr	Thr	Trp	Gly	Ala	Phe	Ser
		35					40					45			
Phe	Pro	Phe	Ile	Phe	Leu	Ala	Thr	Asp	Leu	Thr	Val	Arg	Ile	Phe	Gly
	50					55					60				
Ala	Pro	Leu	Ala	Arg	Arg	Ile	Ile	Phe	Ala	Val	Met	Ile	Pro	Ala	Leu
65					70					75					80
Leu	Ile	Ser	Tyr	Val	Ile	Ser	Ser	Leu	Phe	Tyr	Met	Gly	Ser	Trp	Gln
			85						90					95	
Gly	Phe	Gly	Ala	Leu	Ala	His	Phe	Asn	Leu	Phe	Val	Ala	Arg	Ile	Ala
			100					105					110		
Thr	Ala	Ser	Phe	Met	Ala	Tyr	Ala	Leu	Gly	Gln	Ile	Leu	Asp	Val	His
	115						120						125		
Val	Phe	Asn	Arg	Leu	Arg	Gln	Ser	Arg	Arg	Trp	Trp	Leu	Ala	Pro	Thr
	130					135					140				
Ala	Ser	Thr	Leu	Phe	Gly	Asn	Val	Ser	Asp	Thr	Leu	Ala	Phe	Phe	Phe
145					150					155					160
Ile	Ala	Phe	Trp	Arg	Ser	Pro	Asp	Ala	Phe	Met	Ala	Glu	His	Trp	Met
			165						170					175	
Glu	Ile	Ala	Leu	Val	Asp	Tyr	Cys	Phe	Lys	Val	Leu	Ile	Ser	Ile	Val
	180							185					190		
Phe	Phe	Leu	Pro	Met	Tyr	Gly	Val	Leu	Leu	Asn	Met	Leu	Leu	Lys	Arg
	195					200					205				
Leu	Ala	Asp	Lys	Ser	Glu	Ile	Asn	Ala	Leu	Gln	Ala	Ser			
210						215					220				

<210> 244
 <211> 203
 <212> PRT
 <213> E. Coli

<400> 244

Met	Ile	Arg	Trp	Met	Asn	Glu	Pro	Leu	Trp	Pro	Phe	Ile	Glu	Arg	Lys
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Lys	Ser	Met	Arg	Asn	Leu	Val	Lys	Tyr	Val	Gly	Ile	Gly	Leu	Leu	Val
			20					25					30		
Met	Gly	Leu	Ala	Ala	Cys	Asp	Asp	Lys	Asp	Thr	Asn	Ala	Thr	Ala	Gln
		35					40					45			
Gly	Ser	Val	Ala	Glu	Ser	Asn	Ala	Thr	Gly	Asn	Pro	Val	Asn	Leu	Leu
	50					55					60				
Asp	Gly	Lys	Leu	Ser	Phe	Ser	Leu	Pro	Ala	Asp	Met	Thr	Asp	Gln	Ser

65					70					75					80
Gly	Lys	Leu	Gly	Thr	Gln	Ala	Asn	Asn	Met	His	Val	Trp	Ser	Asp	Ala
				85					90					95	
Thr	Gly	Gln	Lys	Ala	Val	Ile	Val	Ile	Met	Gly	Asp	Asp	Pro	Lys	Glu
			100					105					110		
Asp	Leu	Ala	Val	Leu	Ala	Lys	Arg	Leu	Glu	Asp	Gln	Gln	Arg	Ser	Arg
		115				120					125				
Asp	Pro	Gln	Leu	Gln	Val	Val	Thr	Asn	Lys	Ala	Ile	Glu	Leu	Lys	Gly
	130					135					140				
His	Lys	Met	Gln	Gln	Leu	Asp	Ser	Ile	Ile	Ser	Ala	Lys	Gly	Gln	Thr
145					150					155					160
Ala	Tyr	Ser	Ser	Val	Ile	Leu	Gly	Asn	Val	Gly	Asn	Gln	Leu	Leu	Thr
				165					170					175	
Met	Gln	Ile	Thr	Leu	Pro	Ala	Asp	Asp	Gln	Gln	Lys	Ala	Gln	Thr	Thr
			180				185						190		
Ala	Glu	Asn	Ile	Ile	Asn	Thr	Leu	Val	Ile	Gln					
		195					200								

<210> 245
 <211> 324
 <212> PRT
 <213> E. Coli

<400> 245

Met	Ala	Asn	Met	Phe	Ala	Leu	Ile	Leu	Val	Ile	Ala	Thr	Leu	Val	Thr
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Gly	Ile	Leu	Trp	Cys	Val	Asp	Lys	Phe	Phe	Phe	Ala	Pro	Lys	Arg	Arg
			20					25					30		
Glu	Arg	Gln	Ala	Ala	Ala	Gln	Ala	Ala	Gly	Asp	Ser	Leu	Asp	Lys	
		35				40					45				
Ala	Thr	Leu	Lys	Lys	Val	Ala	Pro	Lys	Pro	Gly	Trp	Leu	Glu	Thr	Gly
	50				55					60					
Ala	Ser	Val	Phe	Pro	Val	Leu	Ala	Ile	Val	Leu	Ile	Val	Arg	Ser	Phe
65				70					75						80
Ile	Tyr	Glu	Pro	Phe	Gln	Ile	Pro	Ser	Gly	Ser	Met	Met	Pro	Thr	Leu
				85					90					95	
Leu	Ile	Gly	Asp	Phe	Ile	Leu	Val	Glu	Lys	Phe	Ala	Tyr	Gly	Ile	Lys
			100					105					110		
Asp	Pro	Ile	Tyr	Gln	Lys	Thr	Leu	Ile	Glu	Thr	Gly	His	Pro	Lys	Arg
		115				120						125			
Gly	Asp	Ile	Val	Val	Phe	Lys	Tyr	Pro	Glu	Asp	Pro	Lys	Leu	Asp	Tyr
	130					135					140				
Ile	Lys	Arg	Ala	Val	Gly	Leu	Pro	Gly	Asp	Lys	Val	Thr	Tyr	Asp	Pro
145					150					155					160
Val	Ser	Lys	Glu	Leu	Thr	Ile	Gln	Pro	Gly	Cys	Ser	Ser	Gly	Gln	Ala
				165					170					175	
Cys	Glu	Asn	Ala	Leu	Pro	Val	Thr	Tyr	Ser	Asn	Val	Glu	Pro	Ser	Asp
		180						185					190		
Phe	Val	Gln	Thr	Phe	Ser	Arg	Arg	Asn	Gly	Gly	Glu	Ala	Thr	Ser	Gly
		195					200					205			
Phe	Phe	Glu	Val	Pro	Lys	Asn	Glu	Thr	Lys	Glu	Asn	Gly	Ile	Arg	Leu
	210					215					220				
Ser	Glu	Arg	Lys	Glu	Thr	Leu	Gly	Asp	Val	Thr	His	Arg	Ile	Leu	Thr
225					230					235					240
Val	Pro	Ile	Ala	Gln	Asp	Gln	Val	Gly	Met	Tyr	Tyr	Gln	Gln	Pro	Gly
				245					250					255	

Gln Gln Leu Ala Thr Trp Ile Val Pro Pro Gly Gln Tyr Phe Met Met
 260 265 270
 Gly Asp Asn Arg Asp Asn Ser Ala Asp Ser Arg Tyr Trp Gly Phe Val
 275 280 285
 Pro Glu Ala Asn Leu Val Gly Arg Ala Thr Ala Ile Trp Met Ser Phe
 290 295 300
 Asp Lys Gln Glu Gly Glu Trp Pro Thr Gly Leu Arg Leu Ser Arg Ile
 305 310 315 320
 Gly Gly Ile His

<210> 246
 <211> 586
 <212> PRT
 <213> E. Coli

<400> 246

Met Thr Ile Thr Lys Leu Ala Trp Arg Asp Leu Val Pro Asp Thr Asp
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 Ser Tyr Gln Glu Ile Phe Ala Gln Pro His Leu Ile Asp Glu Asn Asp
 20 25 30
 Pro Leu Phe Ser Asp Thr Gln Pro Arg Leu Gln Phe Ala Leu Glu Gln
 35 40 45
 Leu Leu His Thr Arg Ala Ser Ser Phe Met Leu Ala Lys Ala Pro
 50 55 60
 Glu Glu Ser Glu Tyr Leu Asn Leu Ile Ala Asn Ala Ala Arg Thr Leu
 65 70 75 80
 Gln Ser Asp Ala Gly Gln Leu Val Gly Gly His Tyr Glu Val Ser Gly
 85 90 95
 His Ser Ile Arg Leu Arg His Ala Val Ser Ala Asp Asp Asn Phe Ala
 100 105 110
 Thr Leu Thr Gln Val Val Ala Ala Asp Trp Val Glu Ala Glu Gln Leu
 115 120 125
 Phe Gly Cys Leu Arg Gln Phe Asn Gly Asp Ile Thr Leu Gln Pro Gly
 130 135 140
 Leu Val His Gln Ala Asn Gly Gly Ile Leu Ile Ile Ser Leu Arg Thr
 145 150 155 160
 Leu Leu Ala Gln Pro Leu Leu Trp Met Arg Leu Lys Asn Ile Val Asn
 165 170 175
 Arg Glu Arg Phe Asp Trp Val Ala Phe Asp Glu Ser Arg Pro Leu Pro
 180 185 190
 Val Ser Val Pro Ser Met Pro Leu Lys Leu Lys Val Ile Leu Val Gly
 195 200 205
 Glu Arg Glu Ser Leu Ala Asp Phe Gln Glu Met Glu Pro Glu Leu Ser
 210 215 220
 Glu Gln Ala Ile Tyr Ser Glu Phe Glu Asp Thr Leu Gln Ile Val Asp
 225 230 235 240
 Ala Glu Ser Val Thr Gln Trp Cys Arg Trp Val Thr Phe Thr Ala Arg
 245 250 255
 His Asn His Leu Pro Ala Pro Gly Ala Asp Ala Trp Pro Ile Leu Ile
 260 265 270
 Arg Glu Ala Ala Arg Tyr Thr Gly Glu Gln Glu Thr Leu Pro Leu Ser
 275 280 285
 Pro Gln Trp Ile Leu Arg Gln Cys Lys Glu Val Ala Ser Leu Cys Asp
 290 295 300

Gly Asp Thr Phe Ser Gly Glu Gln Leu Asn Leu Met Leu Gln Gln Arg
 305 310 315 320
 Glu Trp Arg Glu Gly Phe Leu Ala Glu Arg Met Gln Asp Glu Ile Leu
 325 330 335
 Gln Glu Gln Ile Leu Ile Glu Thr Glu Gly Glu Arg Ile Gly Gln Ile
 340 345 350
 Asn Ala Leu Ser Val Ile Glu Phe Pro Gly His Pro Arg Ala Phe Gly
 355 360 365
 Glu Pro Ser Arg Ile Ser Cys Val Val His Ile Gly Asp Gly Glu Phe
 370 375 380
 Thr Asp Ile Glu Arg Lys Ala Glu Leu Gly Gly Asn Ile His Ala Lys
 385 390 395 400
 Gly Met Met Ile Met Gln Ala Phe Leu Met Ser Glu Leu Gln Leu Glu
 405 410 415
 Gln Gln Ile Pro Phe Ser Ala Ser Leu Thr Phe Glu Gln Ser Tyr Ser
 420 425 430
 Glu Val Asp Gly Asp Ser Ala Ser Met Ala Glu Leu Cys Ala Leu Ile
 435 440 445
 Ser Ala Leu Ala Asp Val Pro Val Asn Gln Ser Ile Ala Ile Thr Gly
 450 455 460
 Ser Val Asp Gln Phe Gly Arg Ala Gln Pro Val Gly Gly Leu Asn Glu
 465 470 475 480
 Lys Ile Glu Gly Phe Phe Ala Ile Cys Gln Gln Arg Glu Leu Thr Gly
 485 490 495
 Lys Gln Gly Val Ile Ile Pro Thr Ala Asn Val Arg His Leu Ser Leu
 500 505 510
 His Ser Glu Leu Val Lys Ala Val Glu Glu Gly Lys Phe Thr Ile Trp
 515 520 525
 Ala Val Asp Asp Val Thr Asp Ala Leu Pro Leu Leu Asn Leu Val
 530 535 540
 Trp Asp Gly Glu Gly Gln Thr Thr Leu Met Gln Thr Ile Gln Glu Arg
 545 550 555 560
 Ile Ala Gln Ala Ser Gln Gln Glu Gly Arg His Arg Phe Pro Trp Pro
 565 570 575
 Leu Arg Trp Leu Asn Trp Phe Ile Pro Asn
 580 585

<210> 247
 <211> 394
 <212> PRT
 <213> E. Coli

<400> 247
 Met Ser Lys Glu Lys Phe Glu Arg Thr Lys Pro His Val Asn Val Gly
 1 5 10 15
 Thr Ile Gly His Val Asp His Gly Lys Thr Thr Leu Thr Ala Ala Ile
 20 25 30
 Thr Thr Val Leu Ala Lys Thr Tyr Gly Gly Ala Ala Arg Ala Phe Asp
 35 40 45
 Gln Ile Asp Asn Ala Pro Glu Glu Lys Ala Arg Gly Ile Thr Ile Asn
 50 55 60
 Thr Ser His Val Glu Tyr Asp Thr Pro Thr Arg His Tyr Ala His Val
 65 70 75 80
 Asp Cys Pro Gly His Ala Asp Tyr Val Lys Asn Met Ile Thr Gly Ala
 85 90 95
 Ala Gln Met Asp Gly Ala Ile Leu Val Val Ala Ala Thr Asp Gly Pro


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      100      105      110
Met Pro Gln Thr Arg Glu His Ile Leu Leu Gly Arg Gln Val Gly Val
      115      120      125
Pro Tyr Ile Ile Val Phe Leu Asn Lys Cys Asp Met Val Asp Asp Glu
      130      135      140
Glu Leu Leu Glu Leu Val Glu Met Glu Val Arg Glu Leu Leu Ser Gln
      145      150      155      160
Tyr Asp Phe Pro Gly Asp Asp Thr Pro Ile Val Arg Gly Ser Ala Leu
      165      170      175
Lys Ala Leu Glu Gly Asp Ala Glu Trp Glu Ala Lys Ile Leu Glu Leu
      180      185      190
Ala Gly Phe Leu Asp Ser Tyr Ile Pro Glu Pro Glu Arg Ala Ile Asp
      195      200      205
Lys Pro Phe Leu Leu Pro Ile Glu Asp Val Phe Ser Ile Ser Gly Arg
      210      215      220
Gly Thr Val Val Thr Gly Arg Val Glu Arg Gly Ile Ile Lys Val Gly
      225      230      235      240
Glu Glu Val Glu Ile Val Gly Ile Lys Glu Thr Gln Lys Ser Thr Cys
      245      250      255
Thr Gly Val Glu Met Phe Arg Lys Leu Leu Asp Glu Gly Arg Ala Gly
      260      265      270
Glu Asn Val Gly Val Leu Leu Arg Gly Ile Lys Arg Glu Glu Ile Glu
      275      280      285
Arg Gly Gln Val Leu Ala Lys Pro Gly Thr Ile Lys Pro His Thr Lys
      290      295      300
Phe Glu Ser Glu Val Tyr Ile Leu Ser Lys Asp Glu Gly Gly Arg His
      305      310      315      320
Thr Pro Phe Phe Lys Gly Tyr Arg Pro Gln Phe Tyr Phe Arg Thr Thr
      325      330      335
Asp Val Thr Gly Thr Ile Glu Leu Pro Glu Gly Val Glu Met Val Met
      340      345      350
Pro Gly Asp Asn Ile Lys Met Val Val Thr Leu Ile His Pro Ile Ala
      355      360      365
Met Asp Asp Gly Leu Arg Phe Ala Ile Arg Glu Gly Gly Arg Thr Val
      370      375      380
Gly Ala Gly Val Val Ala Lys Val Leu Gly
      385      390

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<210> 248
<211> 704
<212> PRT
<213> E. Coli

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      <400> 248
Met Ala Arg Thr Thr Pro Ile Ala Arg Tyr Arg Asn Ile Gly Ile Ser
  1      5      10      15
Ala His Ile Asp Ala Gly Lys Thr Thr Thr Thr Glu Arg Ile Leu Phe
      20      25      30
Tyr Thr Gly Val Asn His Lys Ile Gly Glu Val His Asp Gly Ala Ala
      35      40      45
Thr Met Asp Trp Met Glu Gln Glu Gln Glu Arg Gly Ile Thr Ile Thr
      50      55      60
Ser Ala Ala Thr Thr Ala Phe Trp Ser Gly Met Ala Lys Gln Tyr Glu
      65      70      75      80
Pro His Arg Ile Asn Ile Ile Asp Thr Pro Gly His Val Asp Phe Thr

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				85						90						95	
Ile	Glu	Val	Glu	Arg	Ser	Met	Arg	Val	Leu	Asp	Gly	Ala	Val	Met	Val		
			100					105					110				
Tyr	Cys	Ala	Val	Gly	Gly	Val	Gln	Pro	Gln	Ser	Glu	Thr	Val	Trp	Arg		
		115					120					125					
Gln	Ala	Asn	Lys	Tyr	Lys	Val	Pro	Arg	Ile	Ala	Phe	Val	Asn	Lys	Met		
		130				135					140						
Asp	Arg	Met	Gly	Ala	Asn	Phe	Leu	Lys	Val	Val	Asn	Gln	Ile	Lys	Thr		
145					150					155					160		
Arg	Leu	Gly	Ala	Asn	Pro	Val	Pro	Leu	Gln	Leu	Ala	Ile	Gly	Ala	Glu		
			165						170					175			
Glu	His	Phe	Thr	Gly	Val	Val	Asp	Leu	Val	Lys	Met	Lys	Ala	Ile	Asn		
			180					185				190					
Trp	Asn	Asp	Ala	Asp	Gln	Gly	Val	Thr	Phe	Glu	Tyr	Glu	Asp	Ile	Pro		
		195					200					205					
Ala	Asp	Met	Val	Glu	Leu	Ala	Asn	Glu	Trp	His	Gln	Asn	Leu	Ile	Glu		
		210				215					220						
Ser	Ala	Ala	Glu	Ala	Ser	Glu	Glu	Leu	Met	Glu	Lys	Tyr	Leu	Gly	Gly		
225					230					235					240		
Glu	Glu	Leu	Thr	Glu	Ala	Glu	Ile	Lys	Gly	Ala	Leu	Arg	Gln	Arg	Val		
			245						250					255			
Leu	Asn	Asn	Glu	Ile	Ile	Leu	Val	Thr	Cys	Gly	Ser	Ala	Phe	Lys	Asn		
			260					265					270				
Lys	Gly	Val	Gln	Ala	Met	Leu	Asp	Ala	Val	Ile	Asp	Tyr	Leu	Pro	Ser		
		275					280					285					
Pro	Val	Asp	Val	Pro	Ala	Ile	Asn	Gly	Ile	Leu	Asp	Asp	Gly	Lys	Asp		
		290				295					300						
Thr	Pro	Ala	Glu	Arg	His	Ala	Ser	Asp	Asp	Glu	Pro	Phe	Ser	Ala	Leu		
305					310					315					320		
Ala	Phe	Lys	Ile	Ala	Thr	Asp	Pro	Phe	Val	Gly	Asn	Leu	Thr	Phe	Phe		
			325						330					335			
Arg	Val	Tyr	Ser	Gly	Val	Val	Asn	Ser	Gly	Asp	Thr	Val	Leu	Asn	Ser		
			340					345					350				
Val	Lys	Ala	Ala	Arg	Glu	Arg	Phe	Gly	Arg	Ile	Val	Gln	Met	His	Ala		
		355					360					365					
Asn	Lys	Arg	Glu	Glu	Ile	Lys	Glu	Val	Arg	Ala	Gly	Asp	Ile	Ala	Ala		
		370				375					380						
Ala	Ile	Gly	Leu	Lys	Asp	Val	Thr	Thr	Gly	Asp	Thr	Leu	Cys	Asp	Pro		
385					390					395					400		
Asp	Ala	Pro	Ile	Ile	Leu	Glu	Arg	Met	Glu	Phe	Pro	Glu	Pro	Val	Ile		
			405						410					415			
Ser	Ile	Ala	Val	Glu	Pro	Lys	Thr	Lys	Ala	Asp	Gln	Glu	Lys	Met	Gly		
			420					425									

Ile	Pro	Gly	Glu	Tyr	Ile	Pro	Ala	Val	Asp	Lys	Gly	Ile	Gln	Glu	Gln
545					550					555					560
Leu	Lys	Ala	Gly	Pro	Leu	Ala	Gly	Tyr	Pro	Val	Val	Asp	Met	Gly	Ile
				565					570					575	
Arg	Leu	His	Phe	Gly	Ser	Tyr	His	Asp	Val	Asp	Ser	Ser	Glu	Leu	Ala
			580					585					590		
Phe	Lys	Leu	Ala	Ala	Ser	Ile	Ala	Phe	Lys	Glu	Gly	Phe	Lys	Lys	Ala
		595					600					605			
Lys	Pro	Val	Leu	Leu	Glu	Pro	Ile	Met	Lys	Val	Glu	Val	Glu	Thr	Pro
	610					615					620				
Glu	Glu	Asn	Thr	Gly	Asp	Val	Ile	Gly	Asp	Leu	Ser	Arg	Arg	Arg	Gly
625					630					635					640
Met	Leu	Lys	Gly	Gln	Glu	Ser	Glu	Val	Thr	Gly	Val	Lys	Ile	His	Ala
				645					650					655	
Glu	Val	Pro	Leu	Ser	Glu	Met	Phe	Gly	Tyr	Ala	Thr	Gln	Leu	Arg	Ser
			660					665					670		
Leu	Thr	Lys	Gly	Arg	Ala	Ser	Tyr	Thr	Met	Glu	Phe	Leu	Lys	Tyr	Asp
		675					680					685			
Glu	Ala	Pro	Ser	Asn	Val	Ala	Gln	Ala	Val	Ile	Glu	Ala	Arg	Gly	Lys
	690					695					700				

<210> 249
 <211> 179
 <212> PRT
 <213> E. Coli

<400> 249															
Met	Pro	Arg	Arg	Val	Ile	Gly	Gln	Arg	Lys	Ile	Leu	Pro	Asp	Pro	
1				5				10					15		
Lys	Phe	Gly	Ser	Glu	Leu	Leu	Ala	Lys	Phe	Val	Asn	Ile	Leu	Met	Val
			20					25				30			
Asp	Gly	Lys	Lys	Ser	Thr	Ala	Glu	Ser	Ile	Val	Tyr	Ser	Ala	Leu	Glu
		35					40					45			
Thr	Leu	Ala	Gln	Arg	Ser	Gly	Lys	Ser	Glu	Leu	Glu	Ala	Phe	Glu	Val
	50					55					60				
Ala	Leu	Glu	Asn	Val	Arg	Pro	Thr	Val	Glu	Val	Lys	Ser	Arg	Arg	Val
65					70				75						80
Gly	Gly	Ser	Thr	Tyr	Gln	Val	Pro	Val	Glu	Val	Arg	Pro	Val	Arg	Arg
			85						90				95		
Asn	Ala	Leu	Ala	Met	Arg	Trp	Ile	Val	Glu	Ala	Ala	Arg	Lys	Arg	Gly
		100						105					110		
Asp	Lys	Ser	Met	Ala	Leu	Arg	Leu	Ala	Asn	Glu	Leu	Ser	Asp	Ala	Ala
	115						120					125			
Glu	Asn	Lys	Gly	Thr	Ala	Val	Lys	Lys	Arg	Glu	Asp	Val	His	Arg	Met
	130					135					140				
Ala	Glu	Ala	Asn	Lys	Ala	Phe	Ala	His	Tyr	Arg	Trp	Leu	Ser	Leu	Arg
145					150					155					160
Ser	Phe	Ser	His	Gln	Ala	Gly	Ala	Ser	Ser	Lys	Gln	Pro	Ala	Leu	Gly
			165						170					175	
Tyr	Leu	Asn													

<210> 250
 <211> 124
 <212> PRT

002210-60225460

<213> E. Coli

<400> 250

Met Ala Thr Val Asn Gln Leu Val Arg Lys Pro Arg Ala Arg Lys Val
1 5 10 15
Ala Lys Ser Asn Val Pro Ala Leu Glu Ala Cys Pro Gln Lys Arg Gly
20 25 30
Val Cys Thr Arg Val Tyr Thr Thr Pro Lys Lys Pro Asn Ser Ala
35 40 45
Leu Arg Lys Val Cys Arg Val Arg Leu Thr Asn Gly Phe Glu Val Thr
50 55 60
Ser Tyr Ile Gly Gly Glu Gly His Asn Leu Gln Glu His Ser Val Ile
65 70 75 80
Leu Ile Arg Gly Gly Arg Val Lys Asp Leu Pro Gly Val Arg Tyr His
85 90 95
Thr Val Arg Gly Ala Leu Asp Cys Ser Gly Val Lys Asp Arg Lys Gln
100 105 110
Ala Arg Ser Lys Tyr Gly Val Lys Arg Pro Lys Ala
115 120

<210> 251

<211> 165

<212> PRT

<213> E. Coli

<400> 251

Met Ala Leu Asn Leu Gln Asp Lys Gln Ala Ile Val Ala Glu Val Ser
1 5 10 15
Glu Val Ala Lys Gly Ala Leu Ser Ala Val Val Ala Asp Ser Arg Gly
20 25 30
Val Thr Val Asp Lys Met Thr Glu Leu Arg Lys Ala Gly Arg Glu Ala
35 40 45
Gly Val Tyr Met Arg Val Val Arg Asn Thr Leu Leu Arg Arg Ala Val
50 55 60
Glu Gly Thr Pro Phe Glu Cys Leu Lys Asp Ala Phe Val Gly Pro Thr
65 70 75 80
Leu Ile Ala Tyr Ser Met Glu His Pro Gly Ala Ala Ala Arg Leu Phe
85 90 95
Lys Glu Phe Ala Lys Ala Asn Ala Lys Phe Glu Val Lys Ala Ala Ala
100 105 110
Phe Glu Gly Glu Leu Ile Pro Ala Ser Gln Ile Asp Arg Leu Ala Thr
115 120 125
Leu Pro Thr Tyr Glu Glu Ala Ile Ala Arg Leu Met Ala Thr Met Lys
130 135 140
Glu Ala Ser Ala Gly Lys Leu Val Arg Thr Leu Ala Ala Val Arg Asp
145 150 155 160
Ala Lys Glu Ala Ala
165

<210> 252

<211> 121

<212> PRT

<213> E. Coli

<400> 252

Met Ser Ile Thr Lys Asp Gln Ile Ile Glu Ala Val Ala Ala Met Ser
 1 5 10 15
 Val Met Asp Val Val Glu Leu Ile Ser Ala Met Glu Glu Lys Phe Gly
 20 25 30
 Val Ser Ala Ala Ala Val Ala Val Ala Ala Gly Pro Val Glu Ala
 35 40 45
 Ala Glu Glu Lys Thr Glu Phe Asp Val Ile Leu Lys Ala Ala Gly Ala
 50 55 60
 Asn Lys Val Ala Val Ile Lys Ala Val Arg Gly Ala Thr Gly Leu Gly
 65 70 75 80
 Leu Lys Glu Ala Lys Asp Leu Val Glu Ser Ala Pro Ala Ala Leu Lys
 85 90 95
 Glu Gly Val Ser Lys Asp Asp Ala Glu Ala Leu Lys Lys Ala Leu Glu
 100 105 110
 Glu Ala Gly Ala Glu Val Glu Val Lys
 115 120

<210> 253
 <211> 714
 <212> PRT
 <213> E. Coli

<400> 253

Met Ser Arg Ile Ile Met Leu Ile Pro Thr Gly Thr Ser Val Gly Leu
 1 5 10 15
 Thr Ser Val Ser Leu Gly Val Ile Arg Ala Met Glu Arg Lys Gly Val
 20 25 30
 Arg Leu Ser Val Phe Lys Pro Ile Ala Gln Pro Arg Thr Gly Gly Asp
 35 40 45
 Ala Pro Asp Gln Thr Thr Thr Ile Val Arg Ala Asn Ser Ser Thr Thr
 50 55 60
 Thr Ala Ala Glu Pro Leu Lys Met Ser Tyr Val Glu Gly Leu Leu Ser
 65 70 75 80
 Ser Asn Gln Lys Asp Val Leu Met Glu Glu Ile Val Ala Asn Tyr His
 85 90 95
 Ala Asn Thr Lys Asp Ala Glu Val Val Leu Val Glu Gly Leu Val Pro
 100 105 110
 Thr Arg Lys His Gln Phe Ala Gln Ser Leu Asn Tyr Glu Ile Ala Lys
 115 120 125
 Thr Leu Asn Ala Glu Ile Val Phe Val Met Ser Gln Gly Thr Asp Thr
 130 135 140
 Pro Glu Gln Leu Lys Glu Arg Ile Glu Leu Thr Arg Asn Ser Phe Gly
 145 150 155 160
 Gly Ala Lys Asn Thr Asn Ile Thr Gly Val Ile Val Asn Lys Leu Asn
 165 170 175
 Ala Pro Val Asp Glu Gln Gly Arg Thr Arg Pro Asp Leu Ser Glu Ile
 180 185 190
 Phe Asp Asp Ser Ser Lys Ala Lys Val Asn Asn Val Asp Pro Ala Lys
 195 200 205
 Leu Gln Glu Ser Ser Pro Leu Pro Val Leu Gly Ala Val Pro Trp Ser
 210 215 220
 Phe Asp Leu Ile Ala Thr Arg Ala Ile Asp Met Ala Arg His Leu Asn
 225 230 235 240
 Ala Thr Ile Ile Asn Glu Gly Asp Ile Asn Thr Arg Arg Val Lys Ser
 245 250 255
 Val Thr Phe Cys Ala Arg Ser Ile Pro His Met Leu Glu His Phe Arg

[illegible]

<210> 254
 <211> 588
 <212> PRT
 <213> E. Coli

<400> 254

Met	Asn	Asn	Ser	Ile	Asn	His	Lys	Phe	His	His	Ile	Ser	Arg	Ala	Glu
1				5					10					15	
Tyr	Gln	Glu	Leu	Ala	Val	Ser	Arg	Gly	Asp	Ala	Val	Ala	Asp	Tyr	
			20				25					30			
Ile	Ile	Asp	Asn	Val	Ser	Ile	Leu	Asp	Leu	Ile	Asn	Gly	Gly	Glu	Ile
		35					40					45			
Ser	Gly	Pro	Ile	Val	Ile	Lys	Gly	Arg	Tyr	Ile	Ala	Gly	Val	Gly	Ala
	50					55					60				
Glu	Tyr	Thr	Asp	Ala	Pro	Ala	Leu	Gln	Arg	Ile	Asp	Ala	Arg	Gly	Ala
65					70					75					80
Thr	Ala	Val	Pro	Gly	Phe	Ile	Asp	Ala	His	Leu	His	Ile	Glu	Ser	Ser
				85					90					95	
Met	Met	Thr	Pro	Val	Thr	Phe	Glu	Thr	Ala	Thr	Leu	Pro	Arg	Gly	Leu
			100					105					110		
Thr	Thr	Val	Ile	Cys	Asp	Pro	His	Glu	Ile	Val	Asn	Val	Met	Gly	Glu
		115					120					125			
Ala	Gly	Phe	Ala	Trp	Phe	Ala	Arg	Cys	Ala	Glu	Gln	Ala	Arg	Gln	Asn
	130					135					140				
Gln	Tyr	Leu	Gln	Val	Ser	Ser	Cys	Val	Pro	Ala	Leu	Glu	Gly	Cys	Asp
145					150					155					160
Val	Asn	Gly	Ala	Ser	Phe	Thr	Leu	Glu	Gln	Met	Leu	Ala	Trp	Arg	Asp
				165					170					175	
His	Pro	Gln	Val	Thr	Gly	Leu	Ala	Glu	Met	Met	Asp	Tyr	Pro	Gly	Val
			180					185					190		
Ile	Ser	Gly	Gln	Asn	Ala	Leu	Leu	Asp	Lys	Leu	Asp	Ala	Phe	Arg	His
		195					200					205			
Leu	Thr	Leu	Asp	Gly	His	Cys	Pro	Gly	Leu	Gly	Gly	Lys	Glu	Leu	Asn
	210					215					220				
Ala	Tyr	Ile	Thr	Ala	Gly	Ile	Glu	Asn	Cys	His	Glu	Ser	Tyr	Gln	Leu
225					230					235					240
Glu	Glu	Gly	Arg	Arg	Lys	Leu	Gln	Leu	Gly	Met	Ser	Leu	Met	Ile	Arg
				245					250					255	
Glu	Gly	Ser	Ala	Ala	Arg	Asn	Leu	Asn	Ala	Leu	Ala	Pro	Leu	Ile	Asn
			260					265					270		
Glu	Phe	Asn	Ser	Pro	Gln	Cys	Met	Leu	Cys	Thr	Asp	Asp	Arg	Asn	Pro
		275					280					285			
Trp	Glu	Ile	Ala	His	Glu	Gly	His	Ile	Asp	Ala	Leu	Ile	Arg	Arg	Leu
	290					295					300				
Ile	Glu	Gln	His	Asn	Val	Pro	Leu	His	Val	Ala	Tyr	Arg	Val	Ala	Ser
305					310					315					320
Trp	Ser	Thr	Ala	Arg	His	Phe	Gly	Leu	Asn	His	Leu	Gly	Leu	Leu	Ala
				325					330					335	
Pro	Gly	Lys	Gln	Ala	Asp	Ile	Val	Leu	Leu	Ser	Asp	Ala	Arg	Lys	Val
			340					345					350		
Thr	Val	Gln	Gln	Val	Leu	Val	Lys	Gly	Glu	Pro	Ile	Asp	Ala	Gln	Thr
		355					360					365			
Leu	Gln	Ala	Glu	Glu	Ser	Ala	Arg	Leu	Ala	Gln	Ser	Ala	Pro	Pro	Tyr
	370					375					380				
Gly	Asn	Thr	Ile	Ala	Arg	Gln	Pro	Val	Ser	Ala	Ser	Asp	Phe	Ala	Leu

002210" 60225460

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385          390          395          400
Gln Phe Thr Pro Gly Lys Arg Tyr Arg Val Ile Asp Val Ile His Asn
      405          410          415
Glu Leu Ile Thr His Ser His Ser Ser Val Tyr Ser Glu Asn Gly Phe
      420          425          430
Asp Arg Asp Asp Val Ser Phe Ile Ala Val Leu Glu Arg Tyr Gly Gln
      435          440          445
Arg Leu Ala Pro Ala Cys Gly Leu Leu Gly Gly Phe Gly Leu Asn Glu
      450          455          460
Gly Ala Leu Ala Ala Thr Val Ser His Asp Ser His Asn Ile Val Val
465          470          475          480
Ile Gly Arg Ser Ala Glu Glu Met Ala Leu Ala Val Asn Gln Val Ile
      485          490          495
Gln Asp Gly Gly Gly Leu Cys Val Val Arg Asn Gly Gln Val Gln Ser
      500          505          510
His Leu Pro Leu Pro Ile Ala Gly Leu Met Ser Thr Asp Thr Ala Gln
      515          520          525
Ser Leu Ala Glu Gln Ile Asp Ala Leu Lys Ala Ala Ala Arg Glu Cys
      530          535          540
Gly Pro Leu Pro Asp Glu Pro Phe Ile Gln Met Ala Phe Leu Ser Leu
545          550          555          560
Pro Val Ile Pro Ala Leu Lys Leu Thr Ser Gln Gly Leu Phe Asp Gly
      565          570          575
Glu Lys Phe Ala Phe Thr Thr Leu Glu Val Thr Glu
      580          585

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<210> 255
 <211> 408
 <212> PRT
 <213> E. Coli

<400> 255

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Met Ala Tyr Cys Asn Pro Gly Leu Glu Ser Arg Pro Asn Lys Arg Asn
 1          5          10          15
Ala Leu Arg Arg His Val Val Thr Gly Ile Gly Met Lys Ile Val Ile
      20          25          30
Ala Pro Asp Ser Tyr Lys Glu Ser Leu Ser Ala Ser Glu Val Ala Gln
      35          40          45
Ala Ile Glu Lys Gly Phe Arg Glu Ile Phe Pro Asp Ala Gln Tyr Val
      50          55          60
Ser Val Pro Val Ala Asp Gly Gly Glu Gly Thr Val Glu Ala Met Ile
65          70          75          80
Ala Ala Thr Gln Gly Ala Glu Arg His Ala Trp Val Thr Gly Pro Leu
      85          90          95
Gly Glu Lys Val Asn Ala Ser Trp Gly Ile Ser Gly Asp Gly Lys Thr
      100          105          110
Ala Phe Ile Glu Met Ala Ala Ala Ser Gly Leu Glu Leu Val Pro Ala
      115          120          125
Glu Lys Arg Asp Pro Leu Val Thr Thr Ser Arg Gly Thr Gly Glu Leu
      130          135          140
Ile Leu Gln Ala Leu Glu Ser Gly Ala Thr Asn Ile Ile Ile Gly Ile
145          150          155          160
Gly Gly Ser Ala Thr Asn Asp Gly Gly Ala Gly Met Val Gln Ala Leu
      165          170          175
Gly Ala Lys Leu Cys Asp Ala Asn Gly Asn Glu Ile Gly Phe Gly Gly
      180          185          190

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Gly Ser Leu Asn Thr Leu Asn Asp Ile Asp Ile Ser Gly Leu Asp Pro
 195 200 205
 Arg Leu Lys Asp Cys Val Ile Arg Val Ala Cys Asp Val Thr Asn Pro
 210 215 220
 Leu Val Gly Asp Asn Gly Ala Ser Arg Ile Phe Gly Pro Gln Lys Gly
 225 230 235 240
 Ala Ser Glu Ala Met Ile Val Glu Leu Asp Asn Asn Leu Ser His Tyr
 245 250 255
 Ala Glu Val Ile Lys Lys Ala Leu His Val Asp Val Lys Asp Val Pro
 260 265 270
 Gly Ala Gly Ala Ala Gly Gly Met Gly Ala Ala Leu Met Ala Phe Leu
 275 280 285
 Gly Ala Glu Leu Lys Ser Gly Ile Glu Ile Val Thr Thr Ala Leu Asn
 290 295 300
 Leu Glu Glu His Ile His Asp Cys Thr Leu Val Ile Thr Gly Glu Gly
 305 310 315 320
 Arg Ile Asp Ser Gln Ser Ile His Gly Lys Val Pro Ile Gly Val Ala
 325 330 335
 Asn Val Ala Lys Lys Tyr His Lys Pro Val Ile Gly Ile Ala Gly Ser
 340 345 350
 Leu Thr Asp Asp Val Gly Val Val His Gln His Gly Ile Asp Ala Val
 355 360 365
 Phe Ser Val Leu Thr Ser Ile Gly Thr Leu Asp Glu Ala Phe Arg Gly
 370 375 380
 Ala Tyr Asp Asn Ile Cys Arg Ala Ser Arg Asn Ile Ala Ala Thr Leu
 385 390 395 400
 Ala Ile Gly Met Arg Asn Ala Gly
 405

<210> 256
 <211> 299
 <212> PRT
 <213> E. Coli

<400> 256

Met Ile Asp Met Thr Met Lys Val Gly Phe Ile Gly Leu Gly Ile Met
 1 5 10 15
 Gly Lys Pro Met Ser Lys Asn Leu Leu Lys Ala Gly Tyr Ser Leu Val
 20 25 30
 Val Ala Asp Arg Asn Pro Glu Ala Ile Ala Asp Val Ile Ala Ala Gly
 35 40 45
 Ala Glu Thr Ala Ser Thr Ala Lys Ala Ile Ala Glu Gln Cys Asp Val
 50 55 60
 Ile Ile Thr Met Leu Pro Asn Ser Pro His Val Lys Glu Val Ala Leu
 65 70 75 80
 Gly Glu Asn Gly Ile Glu Gly Ala Lys Pro Gly Thr Val Leu Ile
 85 90 95
 Asp Met Ser Ser Ile Ala Pro Leu Ala Ser Arg Glu Ile Ser Glu Ala
 100 105 110
 Leu Lys Ala Lys Gly Ile Asp Met Leu Asp Ala Pro Val Ser Gly Gly
 115 120 125
 Glu Pro Lys Ala Ile Asp Gly Thr Leu Ser Val Met Val Gly Gly Asp
 130 135 140
 Lys Ala Ile Phe Asp Lys Tyr Tyr Asp Leu Met Lys Ala Met Ala Gly
 145 150 155 160
 Ser Val Val His Thr Gly Glu Ile Gly Ala Gly Asn Val Thr Lys Leu

				165					170					175			
Ala	Asn	Gln	Val	Ile	Val	Ala	Leu	Asn	Ile	Ala	Ala	Met	Ser	Glu	Ala		
			180					185					190				
Leu	Thr	Leu	Ala	Thr	Lys	Ala	Gly	Val	Asn	Pro	Asp	Leu	Val	Tyr	Gln		
		195					200					205					
Ala	Ile	Arg	Gly	Gly	Leu	Ala	Gly	Ser	Thr	Val	Leu	Asp	Ala	Lys	Ala		
	210					215					220						
Pro	Met	Val	Met	Asp	Arg	Asn	Phe	Lys	Pro	Gly	Phe	Arg	Ile	Asp	Leu		
225				230						235					240		
His	Ile	Lys	Asp	Leu	Ala	Asn	Ala	Leu	Asp	Thr	Ser	His	Gly	Val	Gly		
			245						250					255			
Ala	Gln	Leu	Pro	Leu	Thr	Ala	Ala	Val	Met	Glu	Met	Met	Gln	Ala	Leu		
			260					265					270				
Arg	Ala	Asp	Gly	Leu	Gly	Thr	Ala	Asp	His	Ser	Ala	Leu	Ala	Cys	Tyr		
		275					280					285					
Tyr	Glu	Lys	Leu	Ala	Lys	Val	Glu	Val	Thr	Arg							
	290					295											

<210> 257
 <211> 256
 <212> PRT
 <213> E. Coli

<400> 257

Met	Asn	Asn	Asp	Val	Phe	Pro	Asn	Lys	Phe	Lys	Ala	Ala	Leu	Ala	Ala		
1				5					10					15			
Lys	Gln	Val	Gln	Ile	Gly	Cys	Trp	Ser	Ala	Leu	Ser	Asn	Pro	Ile	Ser		
			20					25					30				
Thr	Glu	Val	Leu	Gly	Leu	Ala	Gly	Phe	Asp	Trp	Leu	Val	Leu	Asp	Gly		
		35					40					45					
Glu	His	Ala	Pro	Asn	Asp	Ile	Ser	Thr	Phe	Ile	Pro	Gln	Leu	Met	Ala		
	50				55						60						
Leu	Lys	Gly	Ser	Ala	Ser	Ala	Pro	Val	Val	Arg	Val	Pro	Thr	Asn	Glu		
65				70					75					80			
Pro	Val	Ile	Ile	Lys	Arg	Leu	Leu	Asp	Ile	Gly	Phe	Tyr	Asn	Phe	Leu		
				85					90					95			
Ile	Pro	Phe	Val	Glu	Thr	Lys	Glu	Glu	Ala	Glu	Leu	Ala	Val	Ala	Ser		
			100					105					110				
Thr	Arg	Tyr	Pro	Pro	Glu	Gly	Ile	Arg	Gly	Val	Ser	Val	Ser	His	Arg		
	115					120						125					
Ala	Asn	Met	Phe	Gly	Thr	Val	Ala	Asp	Tyr	Phe	Ala	Gln	Ser	Asn	Lys		
	130					135					140						
Asn	Ile	Thr	Ile	Leu	Val	Gln	Ile	Glu	Ser	Gln	Gln	Gly	Val	Asp	Asn		
145				150						155					160		
Val	Asp	Ala	Ile	Ala	Ala	Thr	Glu	Gly	Val	Asp	Gly	Ile	Phe	Val	Gly		
			165					170						175			
Pro	Ser	Asp	Leu	Ala	Ala	Ala	Leu	Gly	His	Leu	Gly	Asn	Ala	Ser	His		
		180						185					190				
Pro	Asp	Val	Gln	Lys	Ala	Ile	Gln	His	Ile	Phe	Asn	Arg	Ala	Ser	Ala		
		195					200						205				
His	Gly	Lys	Pro	Ser	Gly	Ile	Leu	Ala	Pro	Val	Glu	Ala	Asp	Ala	Arg		
	210					215					220						
Arg	Tyr	Leu	Glu	Trp	Gly	Ala	Thr	Phe	Val	Ala	Val	Gly	Ser	Asp	Leu		
225				230						235					240		
Gly	Val	Phe	Arg	Ser	Ala	Thr	Gln	Lys	Leu	Ala	Asp	Thr	Phe	Lys	Lys		

245

250

255

<210> 258
 <211> 444
 <212> PRT
 <213> E. Coli

<400> 258

Met	Ile	Leu	Asp	Thr	Val	Asp	Glu	Lys	Lys	Lys	Gly	Val	His	Thr	Arg
1				5					10					15	
Tyr	Leu	Ile	Leu	Ile	Ile	Phe	Ile	Val	Thr	Ala	Val	Asn	Tyr	Ala	
			20				25					30			
Asp	Arg	Ala	Thr	Leu	Ser	Ile	Ala	Gly	Thr	Glu	Val	Ala	Lys	Glu	Leu
		35					40					45			
Gln	Leu	Ser	Ala	Val	Ser	Met	Gly	Tyr	Ile	Phe	Ser	Ala	Phe	Gly	Trp
	50					55					60				
Ala	Tyr	Leu	Leu	Met	Gln	Ile	Pro	Gly	Gly	Trp	Leu	Leu	Asp	Lys	Phe
65					70					75					80
Gly	Ser	Lys	Lys	Val	Tyr	Thr	Tyr	Ser	Leu	Phe	Phe	Trp	Ser	Leu	Phe
				85				90						95	
Thr	Phe	Leu	Gln	Gly	Phe	Val	Asp	Met	Phe	Pro	Leu	Ala	Trp	Ala	Gly
			100				105						110		
Ile	Ser	Met	Phe	Phe	Met	Arg	Phe	Met	Leu	Gly	Phe	Ser	Glu	Ala	Pro
		115				120						125			
Ser	Phe	Pro	Ala	Asn	Ala	Arg	Ile	Val	Ala	Ala	Trp	Phe	Pro	Thr	Lys
	130				135						140				
Glu	Arg	Gly	Thr	Ala	Ser	Ala	Ile	Phe	Asn	Ser	Ala	Gln	Tyr	Phe	Ser
145					150					155					160
Leu	Ala	Leu	Phe	Ser	Pro	Leu	Leu	Gly	Trp	Leu	Thr	Phe	Ala	Trp	Gly
				165				170						175	
Trp	Glu	His	Val	Phe	Thr	Val	Met	Gly	Val	Ile	Gly	Phe	Val	Leu	Thr
			180					185					190		
Ala	Leu	Trp	Ile	Lys	Leu	Ile	His	Asn	Pro	Thr	Asp	His	Pro	Arg	Met
	195						200					205			
Ser	Ala	Glu	Glu	Leu	Lys	Phe	Ile	Ser	Glu	Asn	Gly	Ala	Val	Val	Asp
	210				215						220				
Met	Asp	His	Lys	Lys	Pro	Gly	Ser	Ala	Ala	Ala	Ser	Gly	Pro	Lys	Leu
225					230					235					240
His	Tyr	Ile	Lys	Gln	Leu	Leu	Ser	Asn	Arg	Met	Met	Leu	Gly	Val	Phe
				245					250					255	
Phe	Gly	Gln	Tyr	Phe	Ile	Asn	Thr	Ile	Thr	Trp	Phe	Phe	Leu	Thr	Trp
			260				265						270		
Phe	Pro	Ile	Tyr	Leu	Val	Gln	Glu	Lys	Gly	Met	Ser	Ile	Leu	Lys	Val
	275					280						285			
Gly	Leu	Val	Ala	Ser	Ile	Pro	Ala	Leu	Cys	Gly	Phe	Ala	Gly	Gly	Val
	290				295						300				
Leu	Gly	Gly	Val	Phe	Ser	Asp	Tyr	Leu	Ile	Lys	Arg	Gly	Leu	Ser	Leu
305					310					315					320
Thr	Leu	Ala	Arg	Lys	Leu	Pro	Ile	Val	Leu	Gly	Met	Leu	Leu	Ala	Ser
				325					330					335	
Thr	Ile	Ile	Leu	Cys	Asn	Tyr	Thr	Asn	Asn	Thr	Thr	Leu	Val	Val	Met
			340					345					350		
Leu	Met	Ala	Leu	Ala	Phe	Phe	Gly	Lys	Gly	Phe	Gly	Ala	Leu	Gly	Trp
		355					360					365			
Pro	Val	Ile	Ser	Asp	Thr	Ala	Pro	Lys	Glu	Ile	Val	Gly	Leu	Cys	Gly
	370					375					380				

Gly Val Phe Asn Val Phe Gly Asn Val Ala Ser Ile Val Thr Pro Leu
 385 390 395 400
 Val Ile Gly Tyr Leu Val Ser Glu Leu His Ser Phe Asn Ala Ala Leu
 405 410 415
 Val Phe Val Gly Cys Ser Ala Leu Met Ala Met Val Cys Tyr Leu Phe
 420 425 430
 Val Val Gly Asp Ile Lys Arg Met Glu Leu Gln Lys
 435 440

<210> 259
 <211> 511
 <212> PRT
 <213> E. Coli

<400> 259
 Met Gln Thr Ser Asp Thr Arg Ala Leu Pro Leu Leu Cys Ala Arg Ser
 1 5 10 15
 Val Tyr Lys Gln Tyr Ser Gly Val Asn Val Leu Lys Gly Ile Asp Phe
 20 25 30
 Thr Leu His Gln Gly Glu Val His Ala Leu Leu Gly Gly Asn Gly Ala
 35 40 45
 Gly Lys Ser Thr Leu Met Lys Ile Ile Ala Gly Ile Thr Pro Ala Asp
 50 55 60
 Ser Gly Thr Leu Glu Ile Glu Gly Asn Asn Tyr Val Arg Leu Thr Pro
 65 70 75 80
 Val His Ala His Gln Leu Gly Ile Tyr Leu Val Pro Gln Glu Pro Leu
 85 90 95
 Leu Phe Pro Ser Leu Ser Ile Lys Glu Asn Ile Leu Phe Gly Leu Ala
 100 105 110
 Lys Lys Gln Leu Ser Met Gln Lys Met Lys Asn Leu Leu Ala Ala Leu
 115 120 125
 Gly Cys Gln Phe Asp Leu His Ser Leu Ala Gly Ser Leu Asp Val Ala
 130 135 140
 Asp Arg Gln Met Val Glu Ile Leu Arg Gly Leu Met Arg Asp Ser Arg
 145 150 155 160
 Ile Leu Ile Leu Asp Glu Pro Thr Ala Ser Leu Thr Pro Ala Glu Thr
 165 170 175
 Glu Arg Leu Phe Ser Arg Leu Gln Glu Leu Leu Ala Thr Gly Val Gly
 180 185 190
 Ile Val Phe Ile Ser His Lys Leu Pro Glu Ile Arg Gln Ile Ala Asp
 195 200 205
 Arg Ile Ser Val Met Arg Asp Gly Thr Ile Ala Leu Ser Gly Lys Thr
 210 215 220
 Ser Glu Leu Ser Thr Asp Asp Ile Ile Gln Ala Ile Thr Pro Ala Val
 225 230 235 240
 Arg Glu Lys Ser Leu Ser Ala Ser Gln Lys Leu Trp Leu Glu Leu Pro
 245 250 255
 Gly Asn Arg Pro Gln His Ala Ala Gly Thr Pro Val Leu Thr Leu Glu
 260 265 270
 Asn Leu Thr Gly Glu Gly Phe Arg Asn Val Ser Leu Thr Leu Asn Ala
 275 280 285
 Gly Glu Ile Leu Gly Leu Ala Gly Leu Val Gly Ala Gly Arg Thr Glu
 290 295 300
 Leu Ala Glu Thr Leu Tyr Gly Leu Arg Thr Leu Arg Gly Gly Arg Ile
 305 310 315 320
 Met Leu Asn Gly Lys Glu Ile Asn Lys Leu Ser Thr Gly Glu Arg Leu

				325					330					335			
Leu	Arg	Gly	Leu	Val	Tyr	Leu	Pro	Glu	Asp	Arg	Gln	Ser	Ser	Gly	Leu		
			340					345					350				
Asn	Leu	Asp	Ala	Ser	Leu	Ala	Trp	Asn	Val	Cys	Ala	Leu	Thr	His	Asn		
		355					360					365					
Leu	Arg	Gly	Phe	Trp	Ala	Lys	Thr	Ala	Lys	Asp	Asn	Ala	Thr	Leu	Glu		
		370				375					380						
Arg	Tyr	Arg	Arg	Ala	Leu	Asn	Ile	Lys	Phe	Asn	Gln	Pro	Glu	Gln	Ala		
385					390					395					400		
Ala	Arg	Thr	Leu	Ser	Gly	Gly	Asn	Gln	Gln	Lys	Ile	Leu	Ile	Ala	Lys		
			405					410						415			
Cys	Leu	Glu	Ala	Ser	Pro	Gln	Val	Leu	Ile	Val	Asp	Glu	Pro	Thr	Arg		
			420					425					430				
Gly	Val	Asp	Val	Ser	Ala	Arg	Asn	Asp	Ile	Tyr	Gln	Leu	Leu	Arg	Ser		
		435					440					445					
Ile	Ala	Ala	Gln	Asn	Val	Ala	Val	Leu	Leu	Ile	Ser	Ser	Asp	Leu	Glu		
		450				455					460						
Glu	Ile	Glu	Leu	Met	Ala	Asp	Arg	Val	Tyr	Val	Met	His	Gln	Gly	Glu		
465					470					475					480		
Ile	Thr	His	Ser	Ala	Leu	Thr	Glu	Arg	Asp	Ile	Asn	Val	Glu	Thr	Ile		
			485					490						495			
Met	Arg	Val	Ala	Phe	Gly	Asp	Ser	Gln	Arg	Gln	Glu	Ala	Ser	Cys			
			500					505					510				

<210> 260
 <211> 342
 <212> PRT
 <213> E. Coli

				<400> 260													
Met	Leu	Lys	Phe	Ile	Gln	Asn	Asn	Arg	Glu	Ile	Thr	Ala	Leu	Leu	Ala		
1				5					10				15				
Val	Val	Leu	Leu	Phe	Val	Leu	Pro	Gly	Phe	Leu	Asp	Arg	Gln	Tyr	Leu		
			20					25				30					
Ser	Val	Gln	Thr	Leu	Thr	Met	Val	Tyr	Ser	Ser	Ala	Gln	Ile	Leu	Ile		
		35				40					45						
Leu	Leu	Ala	Met	Gly	Ala	Thr	Leu	Val	Met	Leu	Thr	Arg	Asn	Ile	Asp		
		50				55					60						
Val	Ser	Val	Gly	Ser	Ile	Thr	Gly	Met	Cys	Ala	Val	Leu	Leu	Gly	Met		
65				70					75					80			
Leu	Leu	Asn	Ala	Gly	Tyr	Ser	Leu	Pro	Val	Ala	Cys	Val	Ala	Thr	Leu		
			85					90					95				
Leu	Leu	Gly	Leu	Leu	Ala	Gly	Phe	Phe	Asn	Gly	Val	Leu	Val	Ala	Trp		
		100						105					110				
Leu	Lys	Ile	Pro	Ala	Ile	Val	Ala	Thr	Leu	Gly	Thr	Leu	Gly	Leu	Tyr		
		115				120						125					
Arg	Gly	Ile	Met	Leu	Leu	Trp	Thr	Gly	Gly	Lys	Trp	Ile	Glu	Gly	Leu		
	130					135					140						
Pro	Ala	Glu	Leu	Lys	Gln	Leu	Ser	Ala	Pro	Leu	Leu	Leu	Gly	Val	Ser		
145				150						155				160			
Ala	Ile	Gly	Trp	Leu	Thr	Ile	Ile	Leu	Val	Ala	Phe	Met	Ala	Trp	Leu		
			165					170					175				
Leu	Ala	Lys	Thr	Ala	Phe	Gly	Arg	Ser	Phe	Tyr	Ala	Thr	Gly	Asp	Asn		
		180					185						190				
Leu	Gln	Gly	Ala	Arg	Gln	Leu	Gly	Val	Arg	Thr	Glu	Ala	Ile	Arg	Ile		
		195				200						205					

Ala Asn Ile Tyr Gly Gly Ser Gly Ser Ile Ile Gly Thr Ala Ile Ala
 260 265 270
 Val Leu Leu Val Gly Tyr Leu Gln Gln Gly Leu Gln Met Ala Gly Val
 275 280 285
 Pro Asn Gln Val Ser Ser Ala Leu Ser Gly Ala Leu Leu Ile Val Val
 290 295 300
 Val Val Gly Arg Ser Val Ser Leu His Arg Gln Gln Ile Lys Glu Trp
 305 310 315 320
 Leu Ala Arg Arg Ala Asn Asn Pro Leu Pro
 325 330

<210> 262
 <211> 340
 <212> PRT
 <213> E. Coli

<400> 262
 Met Thr Leu His Arg Phe Lys Lys Ile Ala Leu Leu Ser Ala Leu Gly
 1 5 10 15
 Ile Ala Ala Ile Ser Met Asn Val Gln Ala Ala Glu Arg Ile Ala Phe
 20 25 30
 Ile Pro Lys Leu Val Gly Val Gly Phe Phe Thr Ser Gly Gly Asn Gly
 35 40 45
 Ala Gln Gln Ala Gly Lys Glu Leu Gly Val Asp Val Thr Tyr Asp Gly
 50 55 60
 Pro Thr Glu Pro Ser Val Ser Gly Gln Val Gln Leu Ile Asn Asn Phe
 65 70 75 80
 Val Asn Gln Gly Tyr Asn Ala Ile Ile Val Ser Ala Val Ser Pro Asp
 85 90 95
 Gly Leu Cys Pro Ala Leu Lys Arg Ala Met Gln Arg Gly Val Arg Val
 100 105 110
 Leu Thr Trp Asp Ser Asp Thr Lys Pro Glu Cys Arg Ser Tyr Tyr Ile
 115 120 125
 Asn Gln Gly Thr Pro Ala Gln Leu Gly Gly Met Leu Val Asp Met Ala
 130 135 140
 Ala Arg Gln Val Asn Lys Asp Lys Ala Lys Val Ala Phe Phe Tyr Ser
 145 150 155 160
 Ser Pro Thr Val Thr Asp Gln Asn Gln Trp Val Lys Glu Ala Lys Ala
 165 170 175
 Lys Ile Ala Lys Glu His Pro Gly Trp Glu Ile Val Thr Thr Gln Phe
 180 185 190
 Gly Tyr Asn Asp Ala Thr Lys Ser Leu Gln Thr Ala Glu Gly Ile Leu
 195 200 205
 Lys Ala Tyr Ser Asp Leu Asp Ala Ile Ile Ala Pro Asp Ala Asn Ala
 210 215 220
 Leu Pro Ala Ala Ala Gln Ala Ala Glu Asn Leu Lys Asn Asp Lys Val
 225 230 235 240
 Ala Ile Val Gly Phe Ser Thr Pro Asn Val Met Arg Pro Tyr Val Glu
 245 250 255
 Arg Gly Thr Val Lys Glu Phe Gly Leu Trp Asp Val Val Gln Gln Gly
 260 265 270
 Lys Ile Ser Val Tyr Val Ala Asp Ala Leu Leu Lys Lys Gly Ser Met
 275 280 285
 Lys Thr Gly Asp Lys Leu Asp Ile Lys Gly Val Gly Gln Val Glu Val

<212> PRT
<213> E. Coli

<400> 264

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Met His Val Thr Leu Val Glu Ile Asn Val His Glu Asp Lys Val Asp
 1           5           10           15
Glu Phe Ile Glu Val Phe Arg Gln Asn His Leu Gly Ser Val Gln Glu
      20           25           30
Glu Gly Asn Leu Arg Phe Asp Val Leu Gln Asp Pro Glu Val Asn Ser
      35           40           45
Arg Phe Tyr Ile Tyr Glu Ala Tyr Lys Asp Glu Asp Ala Val Ala Phe
      50           55           60
His Lys Thr Thr Pro His Tyr Lys Thr Cys Val Ala Lys Leu Glu Ser
      65           70           75           80
Leu Met Thr Gly Pro Arg Lys Lys Arg Leu Phe Asn Gly Leu Met Pro
      85           90           95

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<210> 265
<211> 383
<212> PRT
<213> E. Coli

<400> 265

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Met Phe Glu Pro Met Glu Leu Thr Asn Asp Ala Val Ile Lys Val Ile
 1           5           10           15
Gly Val Gly Gly Gly Gly Gly Asn Ala Val Glu His Met Val Arg Glu
      20           25           30
Arg Ile Glu Gly Val Glu Phe Phe Ala Val Asn Thr Asp Ala Gln Ala
      35           40           45
Leu Arg Lys Thr Ala Val Gly Gln Thr Ile Gln Ile Gly Ser Gly Ile
      50           55           60
Thr Lys Gly Leu Gly Ala Gly Ala Asn Pro Glu Val Gly Arg Asn Ala
      65           70           75           80
Ala Asp Glu Asp Arg Asp Ala Leu Arg Ala Ala Leu Glu Gly Ala Asp
      85           90           95
Met Val Phe Ile Ala Ala Gly Met Gly Gly Gly Thr Gly Thr Gly Ala
      100          105          110
Ala Pro Val Val Ala Glu Val Ala Lys Asp Leu Gly Ile Leu Thr Val
      115          120          125
Ala Val Val Thr Lys Pro Phe Asn Phe Glu Gly Lys Lys Arg Met Ala
      130          135          140
Phe Ala Glu Gln Gly Ile Thr Glu Leu Ser Lys His Val Asp Ser Leu
      145          150          155          160
Ile Thr Ile Pro Asn Asp Lys Leu Leu Lys Val Leu Gly Arg Gly Ile
      165          170          175
Ser Leu Leu Asp Ala Phe Gly Ala Ala Asn Asp Val Leu Lys Gly Ala
      180          185          190
Val Gln Gly Ile Ala Glu Leu Ile Thr Arg Pro Gly Leu Met Asn Val
      195          200          205
Asp Phe Ala Asp Val Arg Thr Val Met Ser Glu Met Gly Tyr Ala Met
      210          215          220
Met Gly Ser Gly Val Ala Ser Gly Glu Asp Arg Ala Glu Glu Ala Ala
      225          230          235          240
Glu Met Ala Ile Ser Ser Pro Leu Leu Glu Asp Ile Asp Leu Ser Gly
      245          250          255
Ala Arg Gly Val Leu Val Asn Ile Thr Ala Gly Phe Asp Leu Arg Leu

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	260		265		270
Asp	Glu Phe	Glu Thr Val	Gly Asn Thr	Ile Arg Ala	Phe Ala Ser Asp
	275		280		285
Asn	Ala Thr	Val Val Ile	Gly Thr Ser	Leu Asp Pro	Asp Met Asn Asp
	290		295		300
Glu	Leu Arg	Val Thr Val	Val Ala Thr	Gly Ile Gly	Met Asp Lys Arg
305		310		315	320
Pro	Glu Ile	Thr Leu Val	Thr Asn Lys	Gln Val Gln	Gln Pro Val Met
		325		330	335
Asp	Arg Tyr	Gln Gln His	Gly Met Ala	Pro Leu Thr	Gln Glu Gln Lys
	340		345		350
Pro	Val Ala	Lys Val Val	Asn Asp Asn	Ala Pro Gln	Thr Ala Lys Glu
	355		360		365
Pro	Asp Tyr	Leu Asp Ile	Pro Ala Phe	Leu Arg Lys	Gln Ala Asp
	370		375		380

<210> 266
 <211> 1014
 <212> PRT
 <213> E. Coli

	<400> 266
Met	Asp Val Ser Arg Arg Gln Phe Phe Lys Ile Cys Ala Gly Gly Met
1	5 10 15
Ala	Gly Thr Thr Val Ala Ala Leu Gly Phe Ala Pro Lys Gln Ala Leu
	20 25 30
Ala	Gln Ala Arg Asn Tyr Lys Leu Arg Ala Lys Glu Ile Arg Asn
	35 40 45
Thr	Cys Thr Tyr Cys Ser Val Gly Cys Gly Leu Leu Met Tyr Ser Leu
	50 55 60
Gly	Asp Gly Ala Lys Asn Ala Arg Glu Ala Ile Tyr His Ile Glu Gly
65	70 75 80
Asp	Pro Asp His Pro Val Ser Arg Gly Ala Leu Cys Pro Lys Gly Ala
	85 90 95
Gly	Leu Leu Asp Tyr Val Asn Ser Glu Asn Arg Leu Arg Tyr Pro Glu
	100 105 110
Tyr	Arg Ala Pro Gly Ser Asp Lys Trp Gln Arg Ile Ser Trp Glu Glu
	115 120 125
Ala	Phe Ser Arg Ile Ala Lys Leu Met Lys Ala Asp Arg Asp Ala Asn
	130 135 140
Phe	Ile Glu Lys Asn Glu Gln Gly Val Thr Val Asn Arg Trp Leu Ser
145	150 155 160
Thr	Gly Met Leu Cys Ala Ser Gly Ala Ser Asn Glu Thr Gly Met Leu
	165 170 175
Thr	Gln Lys Phe Ala Arg Ser Leu Gly Met Leu Ala Val Asp Asn Gln
	180 185 190
Ala	Arg Val His Gly Pro Thr Val Ala Ser Leu Ala Pro Thr Phe Gly
	195 200 205
Arg	Gly Ala Met Thr Asn His Trp Val Asp Ile Lys Asn Ala Asn Val
	210 215 220
Val	Met Val Met Gly Gly Asn Ala Ala Glu Ala His Pro Val Gly Phe
225	230 235 240
Arg	Trp Ala Met Glu Ala Lys Asn Asn Asn Asp Ala Thr Leu Ile Val
	245 250 255
Val	Asp Pro Arg Phe Thr Arg Thr Ala Ser Val Ala Asp Ile Tyr Ala
	260 265 270

Pro	Ile	Arg	Ser	Gly	Thr	Asp	Ile	Thr	Phe	Leu	Ser	Gly	Val	Leu	Arg
		275					280					285			
Tyr	Leu	Ile	Glu	Asn	Asn	Lys	Ile	Asn	Ala	Glu	Tyr	Val	Lys	His	Tyr
	290					295					300				
Thr	Asn	Ala	Ser	Leu	Leu	Val	Arg	Asp	Asp	Phe	Ala	Phe	Glu	Asp	Gly
305					310					315					320
Leu	Phe	Ser	Gly	Tyr	Asp	Ala	Glu	Lys	Arg	Gln	Tyr	Asp	Lys	Ser	Ser
				325					330					335	
Trp	Asn	Tyr	Gln	Leu	Asp	Glu	Asn	Gly	Tyr	Ala	Lys	Arg	Asp	Glu	Thr
			340					345					350		
Leu	Thr	His	Pro	Arg	Cys	Val	Trp	Asn	Leu	Leu	Lys	Glu	His	Val	Ser
		355					360					365			
Arg	Tyr	Thr	Pro	Asp	Val	Val	Glu	Asn	Ile	Cys	Gly	Thr	Pro	Lys	Ala
	370					375					380				
Asp	Phe	Leu	Lys	Val	Cys	Glu	Val	Leu	Ala	Ser	Thr	Ser	Ala	Pro	Asp
385					390					395					400
Arg	Thr	Thr	Thr	Phe	Leu	Tyr	Ala	Leu	Gly	Trp	Thr	Gln	His	Thr	Val
				405					410					415	
Gly	Ala	Gln	Asn	Ile	Arg	Thr	Met	Ala	Met	Ile	Gln	Leu	Leu	Leu	Gly
			420					425					430		
Asn	Met	Gly	Met	Ala	Gly	Gly	Gly	Val	Asn	Ala	Leu	Arg	Gly	His	Ser
		435					440					445			
Asn	Ile	Gln	Gly	Leu	Thr	Asp	Leu	Gly	Leu	Leu	Ser	Thr	Ser	Leu	Pro
	450					455					460				
Gly	Tyr	Leu	Thr	Leu	Pro	Ser	Glu	Lys	Gln	Val	Asp	Leu	Gln	Ser	Tyr
465					470					475					480
Leu	Glu	Ala	Asn	Thr	Pro	Lys	Ala	Thr	Leu	Ala	Asp	Gln	Val	Asn	Tyr
				485					490					495	
Trp	Ser	Asn	Tyr	Pro	Lys	Phe	Phe	Val	Ser	Leu	Met	Lys	Ser	Phe	Tyr
			500					505					510		
Gly	Asp	Ala	Ala	Gln	Lys	Glu	Asn	Asn	Trp	Gly	Tyr	Asp	Trp	Leu	Pro
		515					520					525			
Lys	Trp	Asp	Gln	Thr	Tyr	Asp	Val	Ile	Lys	Tyr	Phe	Asn	Met	Met	Asp
	530					535					540				
Glu	Gly	Lys	Val	Thr	Gly	Tyr	Phe	Cys	Gln	Gly	Phe	Asn	Pro	Val	Ala
545					550					555					560
Ser	Phe	Pro	Asp	Lys	Asn	Lys	Val	Val	Ser	Cys	Leu	Ser	Lys	Leu	Lys
				565					570					575	
Tyr	Met	Val	Val	Ile	Asp	Pro	Leu	Val	Thr	Glu	Thr	Ser	Thr	Phe	Trp
			580					585					590		
Gln	Asn	His	Gly	Glu	Ser	Asn	Asp	Val	Asp	Pro	Ala	Ser	Ile	Gln	Thr
		595					600					605			
Glu	Val	Phe	Arg	Leu	Pro	Ser	Thr	Cys	Phe	Ala	Glu	Glu	Asp	Gly	Ser
	610					615					620				
Ile															

[illegible]

<400> 267

-112-

100 105 110
 Pro Ser Ala Gly Ala Ile Ile Gln Tyr Ala Asn Gly Ile Val Asp Phe
 115 120 125
 Gln Ser Glu Asn Cys Ile Gly Cys Gly Tyr Cys Ile Ala Gly Cys Pro
 130 135 140
 Phe Asn Ile Pro Arg Leu Asn Lys Glu Asp Asn Arg Val Tyr Lys Cys
 145 150 155 160
 Thr Leu Cys Val Asp Arg Val Ser Val Gly Gln Glu Pro Ala Cys Val
 165 170 175
 Lys Thr Cys Pro Thr Gly Ala Ile His Phe Gly Thr Lys Lys Glu Met
 180 185 190
 Leu Glu Leu Ala Glu Gln Arg Val Ala Lys Leu Lys Ala Arg Gly Tyr
 195 200 205
 Glu His Ala Gly Val Tyr Asn Pro Glu Gly Val Gly Gly Thr His Val
 210 215 220
 Met Tyr Val Leu His His Ala Asp Gln Pro Glu Leu Tyr His Gly Leu
 225 230 235 240
 Pro Lys Asp Pro Lys Ile Asp Thr Ser Val Ser Leu Trp Lys Gly Ala
 245 250 255
 Leu Lys Pro Leu Ala Ala Ala Gly Phe Ile Ala Thr Phe Ala Gly Leu
 260 265 270
 Ile Phe His Tyr Ile Gly Ile Gly Pro Asn Lys Glu Val Asp Asp Asp
 275 280 285
 Glu Glu Asp His His Glu
 290

<210> 268

<211> 217

<212> PRT

<213> E. Coli

<400> 268

Met Ser Lys Ser Lys Met Ile Val Arg Thr Lys Phe Ile Asp Arg Ala
 1 5 10 15
 Cys His Trp Thr Val Val Ile Cys Phe Phe Leu Val Ala Leu Ser Gly
 20 25 30
 Ile Ser Phe Phe Phe Pro Thr Leu Gln Trp Leu Thr Gln Thr Phe Gly
 35 40 45
 Thr Pro Gln Met Gly Arg Ile Leu His Pro Phe Phe Gly Ile Ala Ile
 50 55 60
 Phe Val Ala Leu Met Phe Met Phe Val Arg Phe Val His His Asn Ile
 65 70 75 80
 Pro Asp Lys Lys Asp Ile Pro Trp Leu Leu Asn Ile Val Glu Val Leu
 85 90 95
 Lys Gly Asn Glu His Lys Val Ala Asp Val Gly Lys Tyr Asn Ala Gly
 100 105 110
 Gln Lys Met Met Phe Trp Ser Ile Met Ser Met Ile Phe Val Leu Leu
 115 120 125
 Val Thr Gly Val Ile Ile Trp Arg Pro Tyr Phe Ala Gln Tyr Phe Pro
 130 135 140
 Met Gln Val Val Arg Tyr Ser Leu Leu Ile His Ala Ala Ala Gly Ile
 145 150 155 160
 Ile Leu Ile His Ala Ile Leu Ile His Met Tyr Met Ala Phe Trp Val
 165 170 175
 Lys Gly Ser Ile Lys Gly Met Ile Glu Gly Lys Val Ser Arg Arg Trp
 180 185 190

Ala Lys Lys His His Pro Arg Trp Tyr Arg Glu Ile Glu Lys Ala Glu
 195 200 205
 Ala Lys Lys Glu Ser Glu Glu Gly Ile
 210 215

<210> 269
 <211> 86
 <212> PRT
 <213> E. Coli

<400> 269
 Met Ala Leu Leu Ile Thr Lys Lys Cys Ile Asn Cys Asp Met Cys Glu
 1 5 10 15
 Pro Glu Cys Pro Asn Glu Ala Ile Ser Met Gly Asp His Ile Tyr Glu
 20 25 30
 Ile Asn Ser Asp Lys Cys Thr Glu Cys Val Gly His Tyr Glu Thr Pro
 35 40 45
 Thr Cys Gln Lys Val Cys Pro Ile Pro Asn Thr Ile Val Lys Asp Pro
 50 55 60
 Ala His Val Glu Thr Glu Glu Gln Leu Trp Asp Lys Phe Val Leu Met
 65 70 75 80
 His His Ala Asp Lys Ile
 85

<210> 270
 <211> 400
 <212> PRT
 <213> E. Coli

<400> 270
 Met Gln Ser Val Asp Val Ala Ile Val Gly Gly Gly Met Val Gly Leu
 1 5 10 15
 Ala Val Ala Cys Gly Leu Gln Gly Ser Gly Leu Arg Val Ala Val Leu
 20 25 30
 Glu Gln Arg Val Gln Glu Pro Leu Ala Ala Asn Ala Pro Pro Gln Leu
 35 40 45
 Arg Val Ser Ala Ile Asn Ala Ala Ser Glu Lys Leu Leu Thr Arg Leu
 50 55 60
 Gly Val Trp Gln Asp Ile Leu Ser Arg Arg Ala Ser Cys Tyr His Gly
 65 70 75 80
 Met Glu Val Trp Asp Lys Asp Ser Phe Gly His Ile Ser Phe Asp Asp
 85 90 95
 Gln Ser Met Gly Tyr Ser His Leu Gly His Ile Val Glu Asn Ser Val
 100 105 110
 Ile His Tyr Ala Leu Trp Asn Lys Ala His Gln Ser Ser Asp Ile Thr
 115 120 125
 Leu Leu Ala Pro Ala Glu Leu Gln Gln Val Ala Trp Gly Glu Asn Glu
 130 135 140
 Thr Phe Leu Thr Leu Lys Asp Gly Ser Met Leu Thr Ala Arg Leu Val
 145 150 155 160
 Ile Gly Ala Asp Gly Ala Asn Ser Trp Leu Arg Asn Lys Ala Asp Ile
 165 170 175
 Pro Leu Thr Phe Trp Asp Tyr Gln His His Ala Leu Val Ala Thr Ile
 180 185 190
 Arg Thr Glu Glu Pro His Asp Ala Val Ala Arg Gln Val Phe His Gly

Ser Val Ala His Glu Gly Arg Ala Phe Glu Arg Phe Thr Gln His Gly
 195 200 205
 Pro Leu Ala Met Leu Pro Met Ser Asp Gly Arg Cys Ser Leu Val Trp
 210 215 220
 Cys His Pro Leu Glu Arg Arg Glu Glu Val Leu Ser Trp Ser Asp Glu
 225 230 235 240
 Lys Phe Cys Arg Glu Leu Gln Ser Ala Phe Gly Trp Arg Leu Gly Lys
 245 250 255
 Ile Thr His Ala Gly Lys Arg Ser Ala Tyr Pro Leu Ala Leu Thr His
 260 265 270
 Ala Ala Arg Ser Ile Thr His Arg Thr Val Leu Val Gly Asn Ala Ala
 275 280 285
 Gln Thr Leu His Pro Ile Ala Gly Gln Gly Phe Asn Leu Gly Met Arg
 290 295 300
 Asp Val Met Ser Leu Ala Glu Thr Leu Thr Gln Ala Gln Glu Arg Gly
 305 310 315 320
 Glu Asp Met Gly Asp Tyr Gly Val Leu Cys Arg Tyr Gln Gln Arg Arg
 325 330 335
 Gln Ser Asp Arg Glu Ala Thr Ile Gly Val Thr Asp Ser Leu Val His
 340 345 350
 Leu Phe Ala Asn Arg Trp Ala Pro Leu Val Val Gly Arg Asn Ile Gly
 355 360 365
 Leu Met Thr Met Glu Leu Phe Thr Pro Ala Arg Asp Val Leu Ala Gln
 370 375 380
 Arg Thr Leu Gly Trp Val Ala Arg
 385 390

<210> 272

<211> 441

<212> PRT

<213> E. Coli

<400> 272

Met Ser Glu Ile Ser Arg Gln Glu Phe Gln Arg Arg Arg Gln Ala Leu
 1 5 10 15
 Val Glu Gln Met Gln Pro Gly Ser Ala Ala Leu Ile Phe Ala Ala Pro
 20 25 30
 Glu Val Thr Arg Ser Ala Asp Ser Glu Tyr Pro Tyr Arg Gln Asn Ser
 35 40 45
 Asp Phe Trp Tyr Phe Thr Gly Phe Asn Glu Pro Glu Ala Val Leu Val
 50 55 60
 Leu Ile Lys Ser Asp Asp Thr His Asn His Ser Val Leu Phe Asn Arg
 65 70 75 80
 Val Arg Asp Leu Thr Ala Glu Ile Trp Phe Gly Arg Arg Leu Gly Gln
 85 90 95
 Asp Ala Ala Pro Glu Lys Leu Gly Val Asp Arg Ala Leu Ala Phe Ser
 100 105 110
 Glu Ile Asn Gln Gln Leu Tyr Gln Leu Leu Asn Gly Leu Asp Val Val
 115 120 125
 Tyr His Ala Gln Gly Glu Tyr Ala Tyr Ala Asp Val Ile Val Asn Ser
 130 135 140
 Ala Leu Glu Lys Leu Arg Lys Gly Ser Arg Gln Asn Leu Thr Ala Pro
 145 150 155 160
 Ala Thr Met Ile Asp Trp Arg Pro Val Val His Glu Met Arg Leu Phe
 165 170 175
 Lys Ser Pro Glu Glu Ile Ala Val Leu Arg Arg Ala Gly Glu Ile Thr

			180					185				190			
Ala	Met	Ala	His	Thr	Arg	Ala	Met	Glu	Lys	Cys	Arg	Pro	Gly	Met	Phe
		195					200					205			
Glu	Tyr	His	Leu	Glu	Gly	Glu	Ile	His	His	Glu	Phe	Asn	Arg	His	Gly
	210					215					220				
Ala	Arg	Tyr	Pro	Ser	Tyr	Asn	Thr	Ile	Val	Gly	Ser	Gly	Glu	Asn	Gly
225					230					235					240
Cys	Ile	Leu	His	Tyr	Thr	Glu	Asn	Glu	Cys	Glu	Met	Arg	Asp	Gly	Asp
			245						250					255	
Leu	Val	Leu	Ile	Asp	Ala	Gly	Cys	Glu	Tyr	Lys	Gly	Tyr	Ala	Gly	Asp
		260					265						270		
Ile	Thr	Arg	Thr	Phe	Pro	Val	Asn	Gly	Lys	Phe	Thr	Gln	Ala	Gln	Arg
	275					280						285			
Glu	Ile	Tyr	Asp	Ile	Val	Leu	Glu	Ser	Leu	Glu	Thr	Ser	Leu	Arg	Leu
	290					295					300				
Tyr	Arg	Pro	Gly	Thr	Ser	Ile	Leu	Glu	Val	Thr	Gly	Glu	Val	Val	Arg
305					310					315					320
Ile	Met	Val	Ser	Gly	Leu	Val	Lys	Leu	Gly	Ile	Leu	Lys	Gly	Asp	Val
			325						330					335	
Asp	Glu	Leu	Ile	Ala	Gln	Asn	Ala	His	Arg	Pro	Phe	Phe	Met	His	Gly
		340					345					350			
Leu	Ser	His	Trp	Leu	Gly	Leu	Asp	Val	His	Asp	Val	Gly	Val	Tyr	Gly
	355					360						365			
Gln	Asp	Arg	Ser	Arg	Ile	Leu	Glu	Pro	Gly	Met	Val	Leu	Thr	Val	Glu
	370					375					380				
Pro	Gly	Leu	Tyr	Ile	Ala	Pro	Asp	Ala	Glu	Val	Pro	Glu	Gln	Tyr	Arg
385					390					395					400
Gly	Ile	Gly	Ile	Arg	Ile	Glu	Asp	Asp	Ile	Val	Ile	Thr	Glu	Thr	Gly
			405						410					415	
Asn	Glu	Asn	Leu	Thr	Ala	Ser	Val	Val	Lys	Lys	Pro	Glu	Glu	Ile	Glu
		420					425						430		
Ala	Leu	Met	Val	Ala	Ala	Arg	Lys	Gln							
	435						440								

<210> 273
 <211> 194
 <212> PRT
 <213> E. Coli

<400> 273

Met	Leu	Met	Ser	Ile	Gln	Asn	Glu	Met	Pro	Gly	Tyr	Asn	Glu	Met	Asn
1			5						10				15		
Gln	Tyr	Leu	Asn	Gln	Gln	Gly	Thr	Gly	Leu	Thr	Pro	Ala	Glu	Met	His
	20						25					30			
Gly	Leu	Ile	Ser	Gly	Met	Ile	Cys	Gly	Gly	Asn	Asp	Asp	Ser	Ser	Trp
	35					40					45				
Leu	Pro	Leu	Leu	His	Asp	Leu	Thr	Asn	Glu	Gly	Met	Ala	Phe	Gly	His
	50				55						60				
Glu	Leu	Ala	Gln	Ala	Leu	Arg	Lys	Met	His	Ser	Ala	Thr	Ser	Asp	Ala
65					70					75					80
Leu	Gln	Asp	Asp	Gly	Phe	Leu	Phe	Gln	Leu	Tyr	Leu	Pro	Asp	Gly	Asp
			85					90					95		
Asp	Val	Ser	Val	Phe	Asp	Arg	Ala	Asp	Ala	Leu	Ala	Gly	Trp	Val	Asn
		100					105					110			
His	Phe	Leu	Leu	Gly	Leu	Gly	Val	Thr	Gln	Pro	Lys	Leu	Asp	Lys	Val
		115					120					125			

Thr Gly Glu Thr Gly Glu Ala Ile Asp Asp Leu Arg Asn Ile Ala Gln
 130 135 140
 Leu Gly Tyr Asp Glu Asp Glu Asp Gln Glu Glu Leu Glu Met Ser Leu
 145 150 155 160
 Glu Glu Ile Ile Glu Tyr Val Arg Val Ala Ala Leu Leu Cys His Asp
 165 170 175
 Thr Phe Thr His Pro Gln Pro Thr Ala Pro Glu Val Gln Lys Pro Thr
 180 185 190
 Leu His

<210> 274
 <211> 120
 <212> PRT
 <213> E. Coli

<400> 274
 Met Leu Lys Leu Phe Ala Lys Tyr Thr Ser Ile Gly Val Leu Asn Thr
 1 5 10 15
 Leu Ile His Trp Val Val Phe Gly Val Cys Ile Tyr Val Ala His Thr
 20 25 30
 Asn Gln Ala Leu Ala Asn Phe Ala Gly Phe Val Val Ala Val Ser Phe
 35 40 45
 Ser Phe Phe Ala Asn Ala Lys Phe Thr Phe Lys Ala Ser Thr Thr Thr
 50 55 60
 Met Arg Tyr Met Leu Tyr Val Gly Phe Met Gly Thr Leu Ser Ala Thr
 65 70 75 80
 Val Gly Trp Ala Ala Asp Arg Cys Ala Leu Pro Pro Met Ile Thr Leu
 85 90 95
 Val Thr Phe Ser Ala Ile Ser Leu Val Cys Gly Phe Val Tyr Ser Lys
 100 105 110
 Phe Ile Val Phe Arg Asp Ala Lys
 115 120

<210> 275
 <211> 306
 <212> PRT
 <213> E. Coli

<400> 275
 Met Lys Ile Ser Leu Val Val Pro Val Phe Asn Glu Glu Glu Ala Ile
 1 5 10 15
 Pro Ile Phe Tyr Lys Thr Val Arg Glu Phe Glu Glu Leu Lys Ser Tyr
 20 25 30
 Glu Val Glu Ile Val Phe Ile Asn Asp Gly Ser Lys Asp Ala Thr Glu
 35 40 45
 Ser Ile Ile Asn Ala Leu Ala Val Ser Asp Pro Leu Val Val Pro Leu
 50 55 60
 Ser Phe Thr Arg Asn Phe Gly Lys Glu Pro Ala Leu Phe Ala Gly Leu
 65 70 75 80
 Asp His Ala Thr Gly Asp Ala Ile Ile Pro Ile Asp Val Asp Leu Gln
 85 90 95
 Asp Pro Ile Glu Val Ile Pro His Leu Ile Glu Lys Trp Gln Ala Gly
 100 105 110
 Ala Asp Met Val Leu Ala Lys Arg Ser Asp Arg Ser Thr Asp Gly Arg
 115 120 125

Leu Lys Arg Lys Thr Ala Glu Trp Phe Tyr Lys Leu His Asn Lys Ile
 130 135 140
 Ser Asn Pro Lys Ile Glu Glu Asn Val Gly Asp Phe Arg Leu Met Ser
 145 150 155 160
 Arg Asp Val Val Glu Asn Ile Lys Leu Met Pro Glu Arg Asn Leu Phe
 165 170 175
 Met Lys Gly Ile Leu Ser Trp Val Gly Gly Lys Thr Asp Ile Val Glu
 180 185 190
 Tyr Val Arg Ala Glu Arg Ile Ala Gly Asp Thr Lys Phe Asn Gly Trp
 195 200 205
 Lys Leu Trp Asn Leu Ala Leu Glu Gly Ile Thr Ser Phe Ser Thr Phe
 210 215 220
 Pro Leu Arg Ile Trp Thr Tyr Ile Gly Leu Val Val Ala Ser Val Ala
 225 230 235 240
 Phe Ile Tyr Gly Ala Trp Met Ile Leu Asp Thr Ile Ile Phe Gly Asn
 245 250 255
 Ala Val Arg Gly Tyr Pro Ser Leu Leu Val Ser Ile Leu Phe Leu Gly
 260 265 270
 Gly Ile Gln Met Ile Gly Ile Gly Val Leu Gly Glu Tyr Ile Gly Arg
 275 280 285
 Thr Tyr Ile Glu Thr Lys Lys Arg Pro Lys Tyr Ile Ile Lys Arg Val
 290 295 300
 Lys Lys
 305

<210> 276
 <211> 443
 <212> PRT
 <213> E. Coli

<400> 276

Met Asn Lys Ala Ile Lys Val Ser Leu Tyr Ile Ser Phe Val Leu Ile
 1 5 10 15
 Ile Cys Ala Leu Ser Lys Asn Ile Met Met Leu Asn Thr Ser Asp Phe
 20 25 30
 Gly Arg Ala Ile Lys Pro Leu Ile Glu Asp Ile Pro Ala Phe Thr Tyr
 35 40 45
 Asp Leu Pro Leu Leu Tyr Lys Leu Lys Gly His Ile Asp Ser Ile Asp
 50 55 60
 Ser Tyr Glu Tyr Ile Ser Ser Tyr Ser Tyr Ile Leu Tyr Thr Tyr Val
 65 70 75 80
 Leu Phe Ile Ser Ile Phe Thr Glu Tyr Leu Asp Ala Arg Val Leu Ser
 85 90 95
 Leu Phe Leu Lys Val Ile Tyr Ile Tyr Ser Leu Tyr Ala Ile Phe Thr
 100 105 110
 Ser Tyr Ile Lys Thr Glu Arg Tyr Val Thr Leu Phe Thr Phe Phe Ile
 115 120 125
 Leu Ala Phe Leu Met Cys Ser Ser Ser Thr Leu Ser Met Phe Ala Ser
 130 135 140
 Phe Tyr Gln Glu Gln Ile Val Ile Ile Phe Leu Pro Phe Leu Val Tyr
 145 150 155 160
 Ser Leu Thr Cys Lys Asn Asn Lys Ser Met Leu Leu Leu Phe Phe Ser
 165 170 175
 Leu Leu Ile Ile Ser Thr Ala Lys Asn Gln Phe Ile Leu Thr Pro Leu
 180 185 190
 Ile Val Tyr Ser Tyr Tyr Ile Phe Phe Asp Arg His Lys Leu Ile Ile

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      195              200              205
Lys Ser Val Ile Cys Val Val Cys Leu Leu Ala Ser Ile Phe Ala Ile
  210              215              220
Ser Tyr Ser Lys Gly Val Val Glu Leu Asn Lys Tyr His Ala Thr Tyr
  225              230              235              240
Phe Gly Ser Tyr Leu Tyr Met Lys Asn Asn Gly Tyr Lys Met Pro Ser
      245              250              255
Tyr Val Asp Asp Lys Cys Val Gly Leu Asp Ala Trp Gly Asn Lys Phe
      260              265              270
Asp Ile Ser Phe Gly Ala Thr Pro Thr Glu Val Gly Thr Glu Cys Phe
      275              280              285
Glu Ser His Lys Asp Glu Thr Phe Ser Asn Ala Leu Phe Leu Leu Val
      290              295              300
Ser Lys Pro Ser Thr Ile Phe Lys Leu Pro Phe Asp Asp Gly Val Met
  305              310              315              320
Ser Gln Tyr Lys Glu Asn Tyr Phe His Val Tyr Lys Lys Leu His Val
      325              330              335
Ile Tyr Gly Glu Ser Asn Ile Leu Thr Thr Ile Thr Asn Ile Lys Asp
      340              345              350
Asn Ile Phe Lys Asn Ile Arg Phe Ile Ser Leu Leu Leu Phe Phe Ile
      355              360              365
Ala Ser Ile Phe Ile Arg Asn Asn Lys Ile Lys Ala Ser Leu Phe Val
      370              375              380
Val Ser Leu Phe Gly Ile Ser Gln Phe Tyr Val Ser Phe Phe Gly Glu
  385              390              395              400
Gly Tyr Arg Asp Leu Ser Lys His Leu Phe Gly Met Tyr Phe Ser Phe
      405              410              415
Asp Leu Cys Leu Tyr Ile Thr Val Val Phe Leu Ile Tyr Lys Ile Ile
      420              425              430
Gln Arg Asn Gln Asp Asn Ser Asp Val Lys His
      435              440

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<210> 277
<211> 82
<212> PRT
<213> E. Coli

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      <400> 277
Met Gly Ile Leu Ser Trp Ile Ile Phe Gly Leu Ile Ala Gly Ile Leu
  1              5              10              15
Ala Lys Trp Ile Met Pro Gly Lys Asp Gly Gly Gly Phe Phe Met Thr
      20              25              30
Ile Leu Leu Gly Ile Val Gly Ala Val Val Gly Gly Trp Ile Ser Thr
      35              40              45
Leu Phe Gly Phe Gly Lys Val Asp Gly Phe Asn Phe Gly Ser Phe Val
      50              55              60
Val Ala Val Ile Gly Ala Ile Val Val Leu Phe Ile Tyr Arg Lys Ile
      65              70              75              80
Lys Ser

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<210> 278
<211> 60
<212> PRT

```

<213> E. Coli

<400> 278

```

Met Gly Lys Ala Thr Tyr Thr Val Thr Val Thr Asn Asn Ser Asn Gly
 1          5          10          15
Val Ser Val Asp Tyr Glu Thr Glu Thr Pro Met Thr Leu Leu Val Pro
          20          25          30
Glu Val Ala Ala Glu Val Ile Lys Asp Leu Val Asn Thr Val Arg Ser
          35          40          45
Tyr Asp Thr Glu Asn Glu His Asp Val Cys Gly Trp
 50          55          60

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<210> 279

<211> 119

<212> PRT

<213> E. Coli

<400> 279

```

Met Leu Gln Ile Pro Gln Asn Tyr Ile His Thr Arg Ser Thr Pro Phe
 1          5          10          15
Trp Asn Lys Gln Thr Ala Pro Ala Gly Ile Phe Glu Arg His Leu Asp
          20          25          30
Lys Gly Thr Arg Pro Gly Val Tyr Pro Arg Leu Ser Val Met His Gly
          35          40          45
Ala Val Lys Tyr Leu Gly Tyr Ala Asp Glu His Ser Ala Glu Pro Asp
          50          55          60
Gln Val Ile Leu Ile Glu Ala Gly Gln Phe Ala Val Phe Pro Pro Glu
          65          70          75          80
Lys Trp His Asn Ile Glu Ala Met Thr Asp Asp Thr Tyr Phe Asn Ile
          85          90          95
Asp Phe Phe Val Ala Pro Glu Val Leu Met Glu Gly Ala Gln Gln Arg
          100          105          110
Lys Val Ile His Asn Gly Lys
          115

```

<210> 280

<211> 246

<212> PRT

<213> E. Coli

<400> 280

```

Met Lys Phe Lys Val Ile Ala Leu Ala Ala Leu Met Gly Ile Ser Gly
 1          5          10          15
Met Ala Ala Gln Ala Asn Glu Leu Pro Asp Gly Pro His Ile Val Thr
          20          25          30
Ser Gly Thr Ala Ser Val Asp Ala Val Pro Asp Ile Ala Thr Leu Ala
          35          40          45
Ile Glu Val Asn Val Ala Ala Lys Asp Ala Ala Thr Ala Lys Lys Gln
          50          55          60
Ala Asp Glu Arg Val Ala Gln Tyr Ile Ser Phe Leu Glu Leu Asn Gln
          65          70          75          80
Ile Ala Lys Lys Asp Ile Ser Ser Ala Asn Leu Arg Thr Gln Pro Asp
          85          90          95
Tyr Asp Tyr Gln Asp Gly Lys Ser Ile Leu Lys Gly Tyr Arg Ala Val
          100          105          110

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Arg Thr Val Glu Val Thr Leu Arg Gln Leu Asp Lys Leu Asn Ser Leu
 115 120 125
 Leu Asp Gly Ala Leu Lys Ala Gly Leu Asn Glu Ile Arg Ser Val Ser
 130 135 140
 Leu Gly Val Ala Gln Pro Asp Ala Tyr Lys Asp Lys Ala Arg Lys Ala
 145 150 155 160
 Ala Ile Asp Asn Ala Ile His Gln Ala Gln Glu Leu Ala Asn Gly Phe
 165 170 175
 His Arg Lys Leu Gly Pro Val Tyr Ser Val Arg Tyr His Val Ser Asn
 180 185 190
 Tyr Gln Pro Ser Pro Met Val Arg Met Met Lys Ala Asp Ala Ala Pro
 195 200 205
 Val Ser Ala Gln Glu Thr Tyr Glu Gln Ala Ala Ile Gln Phe Asp Asp
 210 215 220
 Gln Val Asp Val Val Phe Gln Leu Glu Pro Val Asp Gln Gln Pro Ala
 225 230 235 240
 Lys Thr Pro Ala Ala Gln
 245

<210> 281
 <211> 464
 <212> PRT
 <213> E. Coli

<400> 281
 Met Leu Leu Leu Asp Ala Cys Ser Gln Met Cys Pro Ser Phe Arg Arg
 1 5 10 15
 Phe Gln Thr Val Phe His Asn Ser Ser Ile Phe Leu Pro Tyr Trp Leu
 20 25 30
 Ala Thr Leu Val Ser Phe Arg Glu Thr Phe Gln Glu Glu Lys Leu Leu
 35 40 45
 Thr Met Lys Gly Ser Tyr Lys Ser Arg Trp Val Ile Val Ile Val Val
 50 55 60
 Val Ile Ala Ala Ile Ala Ala Phe Trp Phe Trp Gln Gly Arg Asn Asp
 65 70 75 80
 Ser Arg Ser Ala Ala Pro Gly Ala Thr Lys Gln Ala Gln Gln Ser Pro
 85 90 95
 Ala Gly Gly Arg Arg Gly Met Arg Ser Gly Pro Leu Ala Pro Val Gln
 100 105 110
 Ala Ala Thr Ala Val Glu Gln Ala Val Pro Arg Tyr Leu Thr Gly Leu
 115 120 125
 Gly Thr Ile Thr Ala Ala Asn Thr Val Thr Val Arg Ser Arg Val Asp
 130 135 140
 Gly Gln Leu Ile Ala Leu His Phe Gln Glu Gly Gln Gln Val Lys Ala
 145 150 155 160
 Gly Asp Leu Leu Ala Glu Ile Asp Pro Ser Gln Phe Lys Val Ala Leu
 165 170 175
 Ala Gln Ala Gln Gly Gln Leu Ala Lys Asp Lys Ala Thr Leu Ala Asn
 180 185 190
 Ala Arg Arg Asp Leu Ala Arg Tyr Gln Gln Leu Ala Lys Thr Asn Leu
 195 200 205
 Val Ser Arg Gln Glu Leu Asp Ala Gln Gln Ala Leu Val Ser Glu Thr
 210 215 220
 Glu Gly Thr Ile Lys Ala Asp Glu Ala Ser Val Ala Ser Ala Gln Leu
 225 230 235 240
 Gln Leu Asp Trp Ser Arg Ile Thr Ala Pro Val Asp Gly Arg Val Gly

														245								250								255	
Leu	Lys	Gln	Val	Asp	Val	Gly	Asn	Gln	Ile	Ser	Ser	Gly	Asp	Thr	Thr																
				260									265									270									
Gly	Ile	Val	Val	Ile	Thr	Gln	Thr	His	Pro	Ile	Asp	Leu	Val	Phe	Thr																
				275									280									285									
Leu	Pro	Glu	Ser	Asp	Ile	Ala	Thr	Val	Val	Gln	Ala	Gln	Lys	Ala	Gly																
				290									295									300									
Lys	Pro	Leu	Val	Val	Glu	Ala	Trp	Asp	Arg	Thr	Asn	Ser	Lys	Lys	Leu																
305					310									315									320								
Ser	Glu	Gly	Thr	Leu	Leu	Ser	Leu	Asp	Asn	Gln	Ile	Asp	Ala	Thr	Thr																
				325									330									335									
Gly	Thr	Ile	Lys	Val	Lys	Ala	Arg	Phe	Asn	Asn	Gln	Asp	Asp	Ala	Leu																
				340									345									350									
Phe	Pro	Asn	Gln	Phe	Val	Asn	Ala	Arg	Met	Leu	Val	Asp	Thr	Glu	Gln																
				355									360									365									
Asn	Ala	Val	Val	Ile	Pro	Thr	Ala	Ala	Leu	Gln	Met	Gly	Asn	Glu	Gly																
				370									375									380									
His	Phe	Val	Trp	Val	Leu	Asn	Ser	Glu	Asn	Lys	Val	Ser	Lys	His	Leu																
385					390									395									400								
Val	Thr	Pro	Gly	Ile	Gln	Asp	Ser	Gln	Lys	Val	Val	Ile	Arg	Ala	Gly																
				405									410									415									
Ile	Ser	Ala	Gly	Asp	Arg	Val	Val	Thr	Asp	Gly	Ile	Asp	Arg	Leu	Thr																
				420									425									430									
Glu	Gly	Ala	Lys	Val	Glu	Val	Val	Glu	Ala	Gln	Ser	Ala	Thr	Thr	Pro																
				435									440									445									
Glu	Glu	Lys	Ala	Thr	Ser	Arg	Glu	Tyr	Ala	Lys	Lys	Gly	Ala	Arg	Ser																
				450									455									460									

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<210> 282
<211> 1040
<212> PRT
<213> E. Coli
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<400> 282

Met	Gln	Val	Leu	Pro	Ser	Ser	Thr	Gly	Gly	Pro	Ser	Arg	Leu	Phe
1				5				10					15	
Ile	Met	Arg	Pro	Val	Ala	Thr	Thr	Leu	Leu	Met	Val	Ala	Ile	Leu
			20					25					30	
Ala	Gly	Ile	Ile	Gly	Tyr	Arg	Ala	Leu	Pro	Val	Ser	Ala	Leu	Pro
		35					40					45		Glu
Val	Asp	Tyr	Pro	Thr	Ile	Gln	Val	Val	Thr	Leu	Tyr	Pro	Gly	Ala
	50					55					60			Ser
Pro	Asp	Val	Met	Thr	Ser	Ala	Val	Thr	Ala	Pro	Leu	Glu	Arg	Gln
65					70					75				80
Gly	Gln	Met	Ser	Gly	Leu	Lys	Gln	Met	Ser	Ser	Gln	Ser	Ser	Gly
			85						90					95
Ala	Ser	Val	Ile	Thr	Leu	Gln	Phe	Gln	Leu	Thr	Leu	Pro	Leu	Asp
			100					105					110	Val
Ala	Glu	Gln	Glu	Val	Gln	Ala	Ala	Ile	Asn	Ala	Ala	Thr	Asn	Leu
		115					120					125		Leu
Pro	Ser	Asp	Leu	Pro	Asn	Pro	Pro	Val	Tyr	Ser	Lys	Val	Asn	Pro
	130					135					140			Ala
Asp	Pro	Pro	Ile	Met	Thr	Leu	Ala	Val	Thr	Ser	Thr	Ala	Met	Pro
145					150					155				160
Thr	Gln	Val	Glu	Asp	Met	Val	Glu	Thr	Arg	Val	Ala	Gln	Lys	Ile
			165						170					175

Gln Ile Ser Gly Val Gly Leu Val Thr Leu Ser Gly Gly Gln Arg Pro
 180 185 190
 Ala Val Arg Val Lys Leu Asn Ala Gln Ala Ile Ala Ala Leu Gly Leu
 195 200 205
 Thr Ser Glu Thr Val Arg Thr Ala Ile Thr Gly Ala Asn Val Asn Ser
 210 215 220
 Ala Lys Gly Ser Leu Asp Gly Pro Ser Arg Ala Val Thr Leu Ser Ala
 225 230 235 240
 Asn Asp Gln Met Gln Ser Ala Glu Glu Tyr Arg Gln Leu Ile Ile Ala
 245 250 255
 Tyr Gln Asn Gly Ala Pro Ile Arg Leu Gly Asp Val Ala Thr Val Glu
 260 265 270
 Gln Gly Ala Glu Asn Ser Trp Leu Gly Ala Trp Ala Asn Lys Glu Gln
 275 280 285
 Ala Ile Val Met Asn Val Gln Arg Gln Pro Gly Ala Asn Ile Ile Ser
 290 295 300
 Thr Ala Asp Ser Ile Arg Gln Met Leu Pro Gln Leu Thr Glu Ser Leu
 305 310 315 320
 Pro Lys Ser Val Lys Val Thr Val Leu Ser Asp Arg Thr Thr Asn Ile
 325 330 335
 Arg Ala Ser Val Asp Asp Thr Gln Phe Glu Leu Met Met Ala Ile Ala
 340 345 350
 Leu Val Val Met Ile Ile Tyr Leu Phe Leu Arg Asn Ile Pro Ala Thr
 355 360 365
 Ile Ile Pro Gly Val Ala Val Pro Leu Ser Leu Ile Gly Thr Phe Ala
 370 375 380
 Val Met Val Phe Leu Asp Phe Ser Ile Asn Asn Leu Thr Leu Met Ala
 385 390 395 400
 Leu Thr Ile Ala Thr Gly Phe Val Val Asp Asp Ala Ile Val Val Ile
 405 410 415
 Glu Asn Ile Ser Arg Tyr Ile Glu Lys Gly Glu Lys Pro Leu Ala Ala
 420 425 430
 Ala Leu Lys Gly Ala Gly Glu Ile Gly Phe Thr Ile Ile Ser Leu Thr
 435 440 445
 Phe Ser Leu Ile Ala Val Leu Ile Pro Leu Leu Phe Met Gly Asp Ile
 450 455 460
 Val Gly Arg Leu Phe Arg Glu Phe Ala Ile Thr Leu Ala Val Ala Ile
 465 470 475 480
 Leu Ile Ser Ala Val Val Ser Leu Thr Leu Thr Pro Met Met Cys Ala
 485 490 495
 Arg Met Leu Ser Gln Glu Ser Leu Arg Lys Gln Asn Arg Phe Ser Arg
 500 505 510
 Ala Ser Glu Lys Met Phe Asp Arg Ile Ile Ala Ala Tyr Gly Arg Gly
 515 520 525
 Leu Ala Lys Val Leu Asn His Pro Trp Leu Thr Leu Ser Val Ala Leu
 530 535 540
 Ser Thr Leu Leu Leu Ser Val Leu Leu Trp Val Phe Ile Pro Lys Gly
 545 550 555 560
 Phe Phe Pro Val Gln Asp Asn Gly Ile Ile Gln Gly Thr Leu Gln Ala
 565 570 575
 Pro Gln Ser Ser Ser Phe Ala Asn Met Ala Gln Arg Gln Arg Gln Val
 580 585 590
 Ala Asp Val Ile Leu Gln Asp Pro Ala Val Gln Ser Leu Thr Ser Phe
 595 600 605
 Val Gly Val Asp Gly Thr Asn Pro Ser Leu Asn Ser Ala Arg Leu Gln
 610 615 620
 Ile Asn Leu Lys Pro Leu Asp Glu Arg Asp Asp Arg Val Gln Lys Val


```

625          630          635          640
Ile Ala Arg Leu Gln Thr Ala Val Asp Lys Val Pro Gly Val Asp Leu
          645          650          655
Phe Leu Gln Pro Thr Gln Asp Leu Thr Ile Asp Thr Gln Val Ser Arg
          660          665          670
Thr Gln Tyr Gln Phe Thr Leu Gln Ala Thr Ser Leu Asp Ala Leu Ser
          675          680          685
Thr Trp Val Pro Gln Leu Met Glu Lys Leu Gln Gln Leu Pro Gln Leu
          690          695          700
Ser Asp Val Ser Ser Asp Trp Gln Asp Lys Gly Leu Val Ala Tyr Val
705          710          715          720
Asn Val Asp Arg Asp Ser Ala Ser Arg Leu Gly Ile Ser Met Ala Asp
          725          730          735
Val Asp Asn Ala Leu Tyr Asn Ala Phe Gly Gln Arg Leu Ile Ser Thr
          740          745          750
Ile Tyr Thr Gln Ala Asn Gln Tyr Arg Val Val Leu Glu His Asn Thr
          755          760          765
Glu Asn Thr Pro Gly Leu Ala Ala Leu Asp Thr Ile Arg Leu Thr Ser
          770          775          780
Ser Asp Gly Gly Val Val Pro Leu Ser Ser Ile Ala Lys Ile Glu Gln
785          790          795          800
Arg Phe Ala Pro Leu Ser Ile Asn His Leu Asp Gln Phe Pro Val Thr
          805          810          815
Thr Ile Ser Phe Asn Val Pro Asp Asn Tyr Ser Leu Gly Asp Ala Val
          820          825          830
Gln Ala Ile Met Asp Thr Glu Lys Thr Leu Asn Leu Pro Val Asp Ile
          835          840          845
Thr Thr Gln Phe Gln Gly Ser Thr Leu Ala Phe Gln Ser Ala Leu Gly
          850          855          860
Ser Thr Val Trp Leu Ile Val Ala Ala Val Val Ala Met Tyr Ile Val
865          870          875          880
Leu Gly Ile Leu Tyr Glu Ser Phe Ile His Pro Ile Thr Ile Leu Ser
          885          890          895
Thr Leu Pro Thr Ala Gly Val Gly Ala Leu Leu Ala Leu Leu Ile Ala
          900          905          910
Gly Ser Glu Leu Asp Val Ile Ala Ile Ile Gly Ile Ile Leu Leu Ile
          915          920          925
Gly Ile Val Lys Lys Asn Ala Ile Met Met Ile Asp Phe Ala Leu Ala
          930          935          940
Ala Glu Arg Glu Gln Gly Met Ser Pro Arg Glu Ala Ile Tyr Gln Ala
945          950          955          960
Cys Leu Leu Arg Phe Arg Pro Ile Leu Met Thr Thr Leu Ala Ala Leu
          965          970          975
Leu Gly Ala Leu Pro Leu Met Leu Ser Thr Gly Val Gly Ala Glu Leu
          980          985          990
Arg Arg Pro Leu Gly Ile Gly Met Val Gly Gly Leu Ile Val Ser Gln
          995          1000          1005
Val Leu Thr Leu Phe Thr Thr Pro Val Ile Tyr Leu Leu Phe Asp Arg
1010          1015          1020
Leu Ala Leu Trp Thr Lys Ser Arg Phe Ala Arg His Glu Glu Glu Ala
1025          1030          1035          1040

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<210> 283

<211> 1025

<212> PRT

<213> E. Coli

<400> 283

Met	Lys	Phe	Phe	Ala	Leu	Phe	Ile	Tyr	Arg	Pro	Val	Ala	Thr	Ile	Leu
1				5					10					15	
Leu	Ser	Val	Ala	Ile	Thr	Leu	Cys	Gly	Ile	Leu	Gly	Phe	Arg	Met	Leu
			20					25					30		
Pro	Val	Ala	Pro	Leu	Pro	Gln	Val	Asp	Phe	Pro	Val	Ile	Ile	Val	Ser
		35					40					45			
Ala	Ser	Leu	Pro	Gly	Ala	Ser	Pro	Glu	Thr	Met	Ala	Ser	Ser	Val	Ala
	50					55					60				
Thr	Pro	Leu	Glu	Arg	Ser	Leu	Gly	Arg	Ile	Ala	Gly	Val	Ser	Glu	Met
65					70					75					80
Thr	Ser	Ser	Ser	Ser	Leu	Gly	Ser	Thr	Arg	Ile	Ile	Leu	Gln	Phe	Asp
				85					90					95	
Phe	Asp	Arg	Asp	Ile	Asn	Gly	Ala	Ala	Arg	Asp	Val	Gln	Ala	Ala	Ile
			100					105					110		
Asn	Ala	Ala	Gln	Ser	Leu	Leu	Pro	Ser	Gly	Met	Pro	Ser	Arg	Pro	Thr
		115					120					125			
Tyr	Arg	Lys	Ala	Asn	Pro	Ser	Asp	Ala	Pro	Ile	Met	Ile	Leu	Thr	Leu
	130					135					140				
Thr	Ser	Asp	Thr	Tyr	Ser	Gln	Gly	Glu	Leu	Tyr	Asp	Phe	Ala	Ser	Thr
145					150					155					160
Gln	Leu	Ala	Pro	Thr	Ile	Ser	Gln	Ile	Asp	Gly	Val	Gly	Asp	Val	Asp
				165					170					175	
Val	Gly	Gly	Ser	Ser	Leu	Pro	Ala	Val	Arg	Val	Gly	Leu	Asn	Pro	Gln
			180					185					190		
Ala	Leu	Phe	Asn	Gln	Gly	Val	Ser	Leu	Asp	Asp	Val	Arg	Thr	Ala	Val
		195					200					205			
Ser	Asn	Ala	Asn	Val	Arg	Lys	Pro	Gln	Gly	Ala	Leu	Glu	Asp	Gly	Thr
	210					215					220				
His	Arg	Trp	Gln	Ile	Gln	Thr	Asn	Asp	Glu	Leu	Lys	Thr	Ala	Ala	Glu
225				230						235					240
Tyr	Gln	Pro	Leu	Ile	Ile	His	Tyr	Asn	Asn	Gly	Gly	Ala	Val	Arg	Leu
				245					250					255	
Gly	Asp	Val	Ala	Thr	Val	Thr	Asp	Ser	Val	Gln	Asp	Val	Arg	Asn	Ala
			260					265					270		
Gly	Met	Thr	Asn	Ala	Lys	Pro	Ala	Ile	Leu	Leu	Met	Ile	Arg	Lys	Leu
		275					280					285			
Pro	Glu	Ala	Asn	Ile	Ile	Gln	Thr	Val	Asp	Ser	Ile	Arg	Ala	Lys	Leu
	290					295					300				
Pro	Glu	Leu	Gln	Glu	Thr	Ile	Pro	Ala	Ala	Ile	Asp	Leu	Gln	Ile	Ala
305					310					315					320
Gln	Asp	Arg	Ser	Pro	Thr	Ile	Arg	Ala	Ser	Leu	Glu	Glu	Val	Glu	Gln
				325					330					335	
Thr	Leu	Ile	Ile	Ser	Val	Ala	Leu	Val	Ile	Leu	Val	Val	Phe	Leu	Phe
			340					345					350		
Leu	Arg	Ser	Gly	Arg	Ala	Thr	Ile	Ile	Pro	Ala	Val	Ser	Val	Pro	Val
		355					360					365			
Ser	Leu	Ile	Gly	Thr	Phe	Ala	Ala	Met	Tyr	Leu	Cys	Gly	Phe	Ser	Leu
	370					375					380				
Asn	Asn	Leu	Ser	Leu	Met	Ala	Leu	Thr	Ile	Ala	Thr	Gly	Phe	Val	Val
385					390					395					400
Asp	Asp	Ala	Ile	Val	Val	Leu	Glu	Asn	Ile	Ala	Arg	His	Leu	Glu	Ala
			405						410					415	
Gly	Met	Lys	Pro	Leu	Gln	Ala	Ala	Leu	Gln	Gly	Thr	Arg	Glu	Val	Gly
			420					425					430		
Phe	Thr	Val	Leu	Ser	Met	Ser	Leu	Ser	Leu	Val	Ala	Val	Phe	Leu	Pro

[illegible]

Leu Phe Asn Ala Pro Phe Ser Leu Ile Ala Leu Ile Gly Ile Met Leu
 900 905 910
 Leu Ile Gly Ile Val Lys Lys Asn Ala Ile Met Met Val Asp Phe Ala
 915 920 925
 Leu Glu Ala Gln Arg His Gly Asn Leu Thr Pro Gln Glu Ala Ile Phe
 930 935 940
 Gln Ala Cys Leu Leu Arg Phe Arg Pro Ile Met Met Thr Thr Leu Ala
 945 950 955 960
 Ala Leu Phe Gly Ala Leu Pro Leu Val Leu Ser Gly Gly Asp Gly Ser
 965 970 975
 Glu Leu Arg Gln Pro Leu Gly Ile Thr Ile Val Gly Gly Leu Val Met
 980 985 990
 Ser Gln Leu Leu Thr Leu Tyr Thr Thr Pro Val Val Tyr Leu Phe Phe
 995 1000 1005
 Asp Arg Leu Arg Leu Arg Phe Ser Arg Lys Pro Lys Gln Thr Val Thr
 1010 1015 1020
 Glu
 1025

<210> 284
 <211> 471
 <212> PRT
 <213> E. Coli

<400> 284
 Met Thr Asp Leu Pro Asp Ser Thr Arg Trp Gln Leu Trp Ile Val Ala
 1 5 10 15
 Phe Gly Phe Phe Met Gln Ser Leu Asp Thr Thr Ile Val Asn Thr Ala
 20 25 30
 Leu Pro Ser Met Ala Gln Ser Leu Gly Glu Ser Pro Leu His Met His
 35 40 45
 Met Val Ile Val Ser Tyr Val Leu Thr Val Ala Val Met Leu Pro Ala
 50 55 60
 Ser Gly Trp Leu Ala Asp Lys Val Gly Val Arg Asn Ile Phe Phe Thr
 65 70 75 80
 Ala Ile Val Leu Phe Thr Leu Gly Ser Leu Phe Cys Ala Leu Ser Gly
 85 90 95
 Thr Leu Asn Glu Leu Leu Leu Ala Arg Ala Leu Gln Gly Val Gly Gly
 100 105 110
 Ala Met Met Val Pro Val Gly Arg Leu Thr Val Met Lys Ile Val Pro
 115 120 125
 Arg Glu Gln Tyr Met Ala Ala Met Thr Phe Val Thr Leu Pro Gly Gln
 130 135 140
 Val Gly Pro Leu Leu Gly Pro Ala Leu Gly Gly Leu Leu Val Glu Tyr
 145 150 155 160
 Ala Ser Trp His Trp Ile Phe Leu Ile Asn Ile Pro Val Gly Ile Ile
 165 170 175
 Gly Ala Ile Ala Thr Leu Leu Leu Met Pro Asn Tyr Thr Met Gln Thr
 180 185 190
 Arg Arg Phe Asp Leu Ser Gly Phe Leu Leu Leu Ala Val Gly Met Ala
 195 200 205
 Val Leu Thr Leu Ala Leu Asp Gly Ser Lys Gly Thr Gly Leu Ser Pro
 210 215 220
 Leu Thr Ile Ala Gly Leu Val Ala Val Gly Val Val Ala Leu Val Leu
 225 230 235 240
 Tyr Leu Leu His Ala Arg Asn Asn Asn Arg Ala Leu Phe Ser Leu Lys

245								250						255			
Leu	Phe	Arg	Thr	Arg	Thr	Phe	Ser	Leu	Gly	Leu	Ala	Gly	Ser	Phe	Ala		
260				265				270									
Gly	Arg	Ile	Gly	Ser	Gly	Met	Leu	Pro	Phe	Met	Thr	Pro	Val	Phe	Leu		
275				280				285									
Gln	Ile	Gly	Leu	Gly	Phe	Ser	Pro	Phe	His	Ala	Gly	Leu	Met	Met	Ile		
290				295				300									
Pro	Met	Val	Leu	Gly	Ser	Met	Gly	Met	Lys	Arg	Ile	Val	Val	Gln	Val		
305					310				315				320				
Val	Asn	Arg	Phe	Gly	Tyr	Arg	Arg	Val	Leu	Val	Ala	Thr	Thr	Leu	Gly		
				325				330				335					
Leu	Ser	Leu	Val	Thr	Leu	Leu	Phe	Met	Thr	Thr	Ala	Leu	Leu	Gly	Trp		
340				345				350									
Tyr	Tyr	Val	Leu	Pro	Phe	Val	Leu	Phe	Leu	Gln	Gly	Met	Val	Asn	Ser		
355				360				365									
Thr	Arg	Phe	Ser	Ser	Met	Asn	Thr	Leu	Thr	Leu	Lys	Asp	Leu	Pro	Asp		
370				375				380									
Asn	Leu	Ala	Ser	Ser	Gly	Asn	Ser	Leu	Leu	Ser	Met	Ile	Met	Gln	Leu		
385					390				395				400				
Ser	Met	Ser	Ile	Gly	Val	Thr	Ile	Ala	Gly	Leu	Leu	Leu	Gly	Leu	Phe		
				405				410				415					
Gly	Ser	Gln	His	Val	Ser	Val	Asp	Ser	Gly	Thr	Thr	Gln	Thr	Val	Phe		
420				425				430									
Met	Tyr	Thr	Trp	Leu	Ser	Met	Ala	Leu	Ile	Ile	Ala	Leu	Pro	Ala	Phe		
435				440				445									
Ile	Phe	Ala	Arg	Val	Pro	Asn	Asp	Thr	His	Gln	Asn	Val	Ala	Ile	Ser		
450				455				460									
Arg	Arg	Lys	Arg	Ser	Ala	Gln											
465					470												

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<210> 285
<211> 344
<212> PRT
<213> E. Coli
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<400> 285															
Met 1	Glu	Ile	Arg	Ile 5	Met	Leu	Phe	Ile	Leu 10	Met	Met	Met	Val	Met 15	Pro
Val	Ser	Tyr	Ala 20	Ala	Cys	Tyr	Ser	Glu 25	Leu	Ser	Val	Gln 30	His	Asn	Leu
Val	Val	Gln 35	Gly	Asp	Phe	Ala 40	Leu	Thr	Gln	Thr	Gln 45	Met	Ala	Thr	Tyr
Glu 50	His	Asn	Phe	Asn	Asp 55	Ser	Ser	Cys	Val	Ser 60	Thr	Asn	Thr	Ile	Thr
Pro 65	Met	Ser	Pro	Ser	Asp 70	Ile	Ile	Val	Gly 75	Leu	Tyr	Asn	Asp	Thr	Ile 80
Lys	Leu	Asn	Leu 85	His	Phe	Glu	Trp	Thr	Asn 90	Lys	Asn	Asn	Ile	Thr 95	Leu
Ser	Asn	Asn	Gln 100	Thr	Ser	Phe	Thr	Ser 105	Gly	Tyr	Ser	Val 110	Thr	Val	Thr
Pro	Ala 115	Ala	Ser	Asn	Ala	Lys	Val 120	Asn	Val	Ser	Ala 125	Gly	Gly	Gly	Gly
Ser 130	Val	Met	Ile	Asn	Gly 135	Val	Ala	Thr	Leu	Ser 140	Ser	Ala	Ser	Ser	Ser
Thr 145	Arg	Gly	Ser	Ala 150	Ala	Val	Gln	Phe	Leu 155	Leu	Cys	Leu	Leu	Gly	Gly 160

Lys Ser Trp Asp Ala Cys Val Asn Ser Tyr Arg Asn Ala Leu Ala Gln
 165 170 175
 Asn Ala Gly Val Tyr Ser Phe Asn Leu Thr Leu Ser Tyr Asn Pro Ile
 180 185 190
 Thr Thr Thr Cys Lys Pro Asp Asp Leu Leu Ile Thr Leu Asp Ser Ile
 195 200 205
 Pro Val Ser Gln Leu Pro Ala Thr Gly Asn Lys Ala Thr Ile Asn Ser
 210 215 220
 Lys Gln Gly Asp Ile Ile Leu Arg Cys Lys Asn Leu Leu Gly Gln Gln
 225 230 235 240
 Asn Gln Thr Ser Arg Lys Met Gln Val Tyr Leu Ser Ser Ser Asp Leu
 245 250 255
 Leu Thr Asn Ser Asn Thr Ile Leu Lys Gly Ala Glu Asp Asn Gly Val
 260 265 270
 Gly Phe Ile Leu Glu Ser Asn Gly Ser Pro Val Thr Leu Leu Asn Ile
 275 280 285
 Thr Asn Ser Ser Lys Gly Tyr Thr Asn Leu Lys Glu Val Ala Ala Lys
 290 295 300
 Ser Lys Leu Thr Asp Thr Thr Val Ser Ile Pro Ile Thr Ala Ser Tyr
 305 310 315 320
 Tyr Val Tyr Asp Thr Asn Lys Val Lys Ser Gly Ala Leu Glu Ala Thr
 325 330 335
 Ala Leu Ile Asn Val Lys Tyr Asp
 340

<210> 286
 <211> 826
 <212> PRT
 <213> E. Coli

<400> 286
 Met Leu Arg Met Thr Pro Leu Ala Ser Ala Ile Val Ala Leu Leu Leu
 1 5 10 15
 Gly Ile Glu Ala Tyr Ala Ala Glu Glu Thr Phe Asp Thr His Phe Met
 20 25 30
 Ile Gly Gly Met Lys Asp Gln Gln Val Ala Asn Ile Arg Leu Asp Asp
 35 40 45
 Asn Gln Pro Leu Pro Gly Gln Tyr Asp Ile Asp Ile Tyr Val Asn Lys
 50 55 60
 Gln Trp Arg Gly Lys Tyr Glu Ile Ile Val Lys Asp Asn Pro Gln Glu
 65 70 75 80
 Thr Cys Leu Ser Arg Glu Val Ile Lys Arg Leu Gly Ile Asn Ser Asp
 85 90 95
 Asn Phe Ala Ser Gly Lys Gln Cys Leu Thr Phe Glu Gln Leu Val Gln
 100 105 110
 Gly Gly Ser Tyr Thr Trp Asp Ile Gly Val Phe Arg Leu Asp Phe Ser
 115 120 125
 Val Pro Gln Ala Trp Val Glu Glu Leu Glu Ser Gly Tyr Val Pro Pro
 130 135 140
 Glu Asn Trp Glu Arg Gly Ile Asn Ala Phe Tyr Thr Ser Tyr Tyr Leu
 145 150 155 160
 Ser Gln Tyr Tyr Ser Asp Tyr Lys Ala Ser Gly Asn Asn Lys Ser Thr
 165 170 175
 Tyr Val Arg Phe Asn Ser Gly Leu Asn Leu Leu Gly Trp Gln Leu His
 180 185 190
 Ser Asp Ala Ser Phe Ser Lys Thr Asn Asn Asn Pro Gly Val Trp Lys

		195					200					205				
Ser	Asn	Thr	Leu	Tyr	Leu	Glu	Arg	Gly	Phe	Ala	Gln	Leu	Leu	Gly	Thr	
	210					215					220					
Leu	Arg	Val	Gly	Asp	Met	Tyr	Thr	Ser	Ser	Asp	Ile	Phe	Asp	Ser	Val	
225					230					235					240	
Arg	Phe	Arg	Gly	Val	Arg	Leu	Phe	Arg	Asp	Met	Gln	Met	Leu	Pro	Asn	
				245					250					255		
Ser	Lys	Gln	Asn	Phe	Thr	Pro	Arg	Val	Gln	Gly	Ile	Ala	Gln	Ser	Asn	
			260					265					270			
Ala	Leu	Val	Thr	Ile	Glu	Gln	Asn	Gly	Phe	Val	Val	Tyr	Gln	Lys	Glu	
		275					280					285				
Val	Pro	Pro	Gly	Pro	Phe	Ala	Ile	Thr	Asp	Leu	Gln	Leu	Ala	Gly	Gly	
	290					295					300					
Gly	Ala	Asp	Leu	Asp	Val	Ser	Val	Lys	Glu	Ala	Asp	Gly	Ser	Val	Thr	
305					310					315					320	
Thr	Tyr	Leu	Val	Pro	Tyr	Ala	Ala	Val	Pro	Asn	Met	Leu	Gln	Pro	Gly	
				325					330					335		
Val	Ser	Lys	Tyr	Asp	Leu	Ala	Ala	Gly	Arg	Ser	His	Ile	Glu	Gly	Ala	
			340					345				350				
Ser	Lys	Gln	Ser	Asp	Phe	Val	Gln	Ala	Gly	Tyr	Gln	Tyr	Gly	Phe	Asn	
		355					360				365					
Asn	Leu	Leu	Thr	Leu	Tyr	Gly	Gly	Ser	Met	Val	Ala	Asn	Asn	Tyr	Tyr	
	370					375					380					
Ala	Phe	Thr	Leu	Gly	Ala	Gly	Trp	Asn	Thr	Arg	Ile	Gly	Ala	Ile	Ser	
385					390					395					400	
Val	Asp	Ala	Thr	Lys	Ser	His	Ser	Lys	Gln	Asp	Asn	Gly	Asp	Val	Phe	
				405					410					415		
Asp	Gly	Gln	Ser	Tyr	Gln	Ile	Ala	Tyr	Asn	Lys	Phe	Val	Ser	Gln	Thr	
			420					425				430				
Ser	Thr	Arg	Phe	Gly	Leu	Ala	Ala	Trp	Arg	Tyr	Ser	Ser	Arg	Asp	Tyr	
		435					440					445				
Arg	Thr	Phe	Asn	Asp	His	Val	Trp	Ala	Asn	Asn	Lys	Asp	Asn	Tyr	Arg	
	450					455					460					
Arg	Asp	Glu	Asn	Asp	Val	Tyr	Asp	Ile	Ala	Asp	Tyr	Tyr	Gln	Asn	Asp	
465					470					475					480	
Phe	Gly	Arg	Lys	Asn	Ser	Phe	Ser	Ala	Asn	Met	Ser	Gln	Ser	Leu	Pro	
				485					490					495		
Glu	Gly	Trp	Gly	Ser	Val	Ser	Leu	Ser	Thr	Leu	Trp	Arg	Asp	Tyr	Trp	
			500					505				510				
Gly	Arg	Ser	Gly	Ser	Ser	Lys	Asp	Tyr	Gln	Leu	Ser	Tyr	Ser	Asn	Asn	
		515					520					525				
Leu	Arg	Arg	Ile	Ser	Tyr	Thr	Leu	Ala	Ala	Ser	Gln	Ala	Tyr	Asp	Glu	
	530					535					540					
Asn	His	His	Glu	Glu	Lys	Arg	Phe	Asn	Ile	Phe	Ile	Ser	Ile	Pro	Phe	
545					550											

Trp Ser Gly Gly Val Asn Leu Ala Asn Arg Leu Ser Glu Thr Phe Ala
 660 665 670
 Val Met Asn Ala Pro Gly Ile Lys Asp Ala Tyr Val Asn Gly Gln Lys
 675 680 685
 Tyr Arg Thr Thr Asn Arg Asn Gly Val Val Ile Tyr Asp Gly Met Thr
 690 695 700
 Pro Tyr Arg Glu Asn His Leu Met Leu Asp Val Ser Gln Ser Asp Ser
 705 710 715 720
 Glu Ala Glu Leu Arg Gly Asn Arg Lys Ile Ala Ala Pro Tyr Arg Gly
 725 730 735
 Ala Val Val Leu Val Asn Phe Asp Thr Asp Gln Arg Lys Pro Trp Phe
 740 745 750
 Ile Lys Ala Leu Arg Ala Asp Gly Gln Ser Leu Thr Phe Gly Tyr Glu
 755 760 765
 Val Asn Asp Ile His Gly His Asn Ile Gly Val Val Gly Gln Gly Ser
 770 775 780
 Gln Leu Phe Ile Arg Thr Asn Glu Val Pro Pro Ser Val Asn Val Ala
 785 790 795 800
 Ile Asp Lys Gln Gln Gly Leu Ser Cys Thr Ile Thr Phe Gly Lys Glu
 805 810 815
 Ile Asp Glu Ser Arg Asn Tyr Ile Cys Gln
 820 825

<210> 287
 <211> 239
 <212> PRT
 <213> E. Coli

<400> 287
 Met Ala Ala Ile Pro Trp Arg Pro Phe Asn Leu Arg Gly Ile Lys Met
 1 5 10 15
 Lys Gly Leu Leu Ser Leu Leu Ile Phe Ser Met Val Leu Pro Ala His
 20 25 30
 Ala Gly Ile Val Ile Tyr Gly Thr Arg Ile Ile Tyr Pro Ala Glu Asn
 35 40 45
 Lys Glu Val Met Val Gln Leu Met Asn Gln Gly Asn Arg Ser Ser Leu
 50 55 60
 Leu Gln Ala Trp Ile Asp Asp Gly Asp Thr Ser Leu Pro Pro Glu Lys
 65 70 75 80
 Ile Gln Val Pro Phe Met Leu Thr Pro Pro Val Ala Lys Ile Gly Ala
 85 90 95
 Asn Ser Gly Gln Gln Val Lys Ile Lys Ile Met Pro Asn Lys Leu Pro
 100 105 110
 Thr Asn Lys Glu Ser Ile Phe Tyr Leu Asn Val Leu Asp Ile Pro Pro
 115 120 125
 Asn Ser Pro Glu Gln Glu Gly Lys Asn Ala Leu Lys Phe Ala Met Gln
 130 135 140
 Asn Arg Ile Lys Leu Phe Tyr Arg Pro Ala Gly Ile Ala Pro Val Asn
 145 150 155 160
 Lys Ala Thr Phe Lys Lys Leu Leu Val Asn Arg Ser Gly Asn Gly Leu
 165 170 175
 Val Ile Lys Asn Asp Ser Ala Asn Trp Val Thr Ile Ser Asp Val Lys
 180 185 190
 Ala Asn Asn Val Lys Val Asn Tyr Glu Thr Ile Met Ile Ala Pro Leu
 195 200 205
 Glu Ser Gln Ser Val Asn Val Lys Ser Asn Asn Ala Asn Asn Trp His

210 215 220
 Leu Thr Ile Ile Asp Asp His Gly Asn Tyr Ile Ser Asp Lys Ile
 225 230 235

<210> 288
 <211> 180
 <212> PRT
 <213> E. Coli

<400> 288
 Met Lys Arg Ser Ile Ile Ala Ala Ala Val Phe Ser Ser Phe Phe Met
 1 5 10 15
 Ser Ala Gly Val Phe Ala Ala Asp Val Asp Thr Gly Thr Leu Thr Ile
 20 25 30
 Lys Gly Asn Ile Ala Glu Ser Pro Cys Lys Phe Glu Ala Gly Gly Asp
 35 40 45
 Ser Val Ser Ile Asn Met Pro Thr Val Pro Thr Ser Val Phe Glu Gly
 50 55 60
 Lys Ala Lys Tyr Ser Thr Tyr Asp Asp Ala Val Gly Val Thr Ser Ser
 65 70 75 80
 Met Leu Lys Ile Ser Cys Pro Lys Glu Val Ala Gly Val Lys Leu Ser
 85 90 95
 Leu Ile Thr Asn Asp Lys Ile Thr Gly Asn Asp Lys Ala Ile Ala Ser
 100 105 110
 Ser Asn Asp Thr Val Gly Tyr Tyr Leu Tyr Leu Gly Asp Asn Ser Asp
 115 120 125
 Val Leu Asp Val Ser Ala Pro Phe Asn Ile Glu Ser Tyr Lys Thr Ala
 130 135 140
 Glu Gly Gln Tyr Ala Ile Pro Phe Lys Ala Lys Tyr Leu Lys Leu Thr
 145 150 155 160
 Asp Asn Ser Val Gln Ser Gly Asp Val Leu Ser Ser Leu Val Met Arg
 165 170 175
 Val Ala Gln Asp
 180

<210> 289
 <211> 112
 <212> PRT
 <213> E. Coli

<400> 289
 Met Ser Ser Glu Arg Asp Leu Val Asn Phe Leu Gly Asp Phe Ser Met
 1 5 10 15
 Asp Val Ala Lys Ala Val Ile Ala Gly Gly Val Ala Thr Ala Ile Gly
 20 25 30
 Ser Leu Ala Ser Phe Ala Cys Val Ser Phe Gly Phe Pro Val Ile Leu
 35 40 45
 Val Gly Gly Ala Ile Leu Leu Thr Gly Ile Val Cys Thr Val Val Leu
 50 55 60
 Asn Glu Ile Asp Ala Gln Cys His Leu Ser Glu Lys Leu Lys Tyr Ala
 65 70 75 80
 Ile Arg Asp Gly Leu Lys Arg Gln Gln Glu Leu Asp Lys Trp Lys Arg
 85 90 95
 Glu Asn Met Thr Pro Phe Met Tyr Val Leu Asn Thr Pro Pro Val Ile

100

105

110

<210> 290
 <211> 193
 <212> PRT
 <213> E. Coli

<400> 290

Met	Thr	Asp	Tyr	Leu	Leu	Leu	Phe	Val	Gly	Thr	Val	Leu	Val	Asn	Asn
1				5					10					15	
Phe	Val	Leu	Val	Lys	Phe	Leu	Gly	Leu	Cys	Pro	Phe	Met	Gly	Val	Ser
			20					25					30		
Lys	Lys	Leu	Glu	Thr	Ala	Met	Gly	Met	Gly	Leu	Ala	Thr	Thr	Phe	Val
			35				40						45		
Met	Thr	Leu	Ala	Ser	Ile	Cys	Ala	Trp	Leu	Ile	Asp	Thr	Trp	Ile	Leu
						55					60				
Ile	Pro	Leu	Asn	Leu	Ile	Tyr	Leu	Arg	Thr	Leu	Ala	Phe	Ile	Leu	Val
65					70					75				80	
Ile	Ala	Val	Val	Val	Gln	Phe	Thr	Glu	Met	Val	Val	Arg	Lys	Thr	Ser
					85				90					95	
Pro	Val	Leu	Tyr	Arg	Leu	Leu	Gly	Ile	Phe	Leu	Pro	Leu	Ile	Thr	Thr
			100					105					110		
Asn	Cys	Ala	Val	Leu	Gly	Val	Ala	Leu	Leu	Asn	Ile	Asn	Leu	Gly	His
		115					120					125			
Asn	Phe	Leu	Gln	Ser	Ala	Leu	Tyr	Gly	Phe	Ser	Ala	Ala	Val	Gly	Phe
		130				135					140				
Ser	Leu	Val	Met	Val	Leu	Phe	Ala	Ala	Ile	Arg	Glu	Arg	Leu	Ala	Val
145					150					155					160
Ala	Asp	Val	Pro	Ala	Pro	Phe	Arg	Gly	Asn	Ala	Ile	Ala	Leu	Ile	Thr
				165					170					175	
Ala	Gly	Leu	Met	Ser	Leu	Ala	Phe	Met	Gly	Phe	Ser	Gly	Leu	Val	Lys
			180					185					190		
Leu															

<210> 291
 <211> 192
 <212> PRT
 <213> E. Coli

<400> 291

Met	Asn	Ala	Ile	Trp	Ile	Ala	Val	Ala	Ala	Val	Ser	Leu	Leu	Gly	Leu
1				5					10					15	
Ala	Phe	Gly	Ala	Ile	Leu	Gly	Tyr	Ala	Ser	Arg	Arg	Phe	Ala	Val	Glu
			20					25					30		
Asp	Asp	Pro	Val	Val	Glu	Lys	Ile	Asp	Glu	Ile	Leu	Pro	Gln	Ser	Gln
			35				40						45		
Cys	Gly	Gln	Cys	Gly	Tyr	Pro	Gly	Cys	Arg	Pro	Tyr	Ala	Glu	Ala	Ile
			50			55					60				
Ser	Cys	Asn	Gly	Glu	Lys	Ile	Asn	Arg	Cys	Ala	Pro	Gly	Gly	Glu	Ala
65					70				75					80	
Val	Met	Leu	Lys	Ile	Ala	Glu	Leu	Leu	Asn	Val	Glu	Pro	Gln	Pro	Leu
					85				90					95	
Asp	Gly	Glu	Ala	Gln	Glu	Ile	Thr	Pro	Ala	Arg	Met	Val	Ala	Val	Ile

			100					105					110				
Asp	Glu	Asn	Asn	Cys	Ile	Gly	Cys	Thr	Lys	Cys	Ile	Gln	Ala	Cys	Pro		
		115					120					125					
Val	Asp	Ala	Ile	Val	Gly	Ala	Thr	Arg	Ala	Met	His	Thr	Val	Met	Ser		
		130					135					140					
Asp	Leu	Cys	Thr	Gly	Cys	Asn	Leu	Cys	Val	Asp	Pro	Cys	Pro	Thr	His		
145					150					155					160		
Cys	Ile	Ser	Leu	Gln	Pro	Val	Ala	Glu	Thr	Pro	Asp	Ser	Trp	Lys	Trp		
				165					170					175			
Asp	Leu	Asn	Thr	Ile	Pro	Val	Arg	Ile	Ile	Pro	Val	Glu	His	His	Ala		
			180					185					190				

<210> 292

<211> 740

<212> PRT

<213> E. Coli

<400> 292

Met	Leu	Lys	Leu	Phe	Ser	Ala	Phe	Arg	Lys	Asn	Lys	Ile	Trp	Asp	Phe		
1				5					10					15			
Asn	Gly	Gly	Ile	His	Pro	Pro	Glu	Met	Lys	Thr	Gln	Ser	Asn	Gly	Thr		
			20					25					30				
Pro	Leu	Arg	Gln	Val	Pro	Leu	Ala	Gln	Arg	Phe	Val	Ile	Pro	Leu	Lys		
		35					40					45					
Gln	His	Ile	Gly	Ala	Glu	Gly	Glu	Leu	Cys	Val	Ser	Val	Gly	Asp	Lys		
50					55					60							
Val	Leu	Arg	Gly	Gln	Pro	Leu	Thr	Arg	Gly	Arg	Gly	Lys	Met	Leu	Pro		
65					70				75					80			
Val	His	Ala	Pro	Thr	Ser	Gly	Thr	Val	Thr	Ala	Ile	Ala	Pro	His	Ser		
				85					90					95			
Thr	Ala	His	Pro	Ser	Ala	Leu	Ala	Glu	Leu	Ser	Val	Ile	Ile	Asp	Ala		
			100					105					110				
Asp	Gly	Glu	Asp	Cys	Trp	Ile	Pro	Arg	Asp	Gly	Trp	Ala	Asp	Tyr	Arg		
		115					120					125					
Thr	Arg	Ser	Arg	Glu	Glu	Leu	Ile	Glu	Arg	Ile	His	Gln	Phe	Gly	Val		
		130				135					140						
Ala	Gly	Leu	Gly	Gly	Ala	Gly	Phe	Pro	Thr	Gly	Val	Lys	Leu	Gln	Gly		
145				150					155					160			
Gly	Gly	Asp	Lys	Ile	Glu	Thr	Leu	Ile	Ile	Asn	Ala	Ala	Glu	Cys	Glu		
				165					170					175			
Pro	Tyr	Ile	Thr	Ala	Asp	Asp	Arg	Leu	Met	Gln	Asp	Cys	Ala	Ala	Gln		
		180					185					190					
Val	Val	Glu	Gly	Ile	Arg	Ile	Leu	Ala	His	Ile	Leu	Gln	Pro	Arg	Glu		
		195					200					205					
Ile	Leu	Ile	Gly	Ile	Glu	Asp	Asn	Lys	Pro	Gln	Ala	Ile	Ser	Met	Leu		
	210				215					220							
Arg	Ala	Val	Leu	Ala	Asp	Ser	Asn	Asp	Ile	Ser	Leu	Arg	Val	Ile	Pro		
225				230					235					240			
Thr	Lys	Tyr	Pro	Ser	Gly	Gly	Ala	Lys	Gln	Leu	Thr	Tyr	Ile	Leu	Thr		
				245					250					255			
Gly	Lys	Gln	Val	Pro	His	Gly	Gly	Arg	Ser	Ser	Asp	Ile	Gly	Val	Leu		
		260					265					270					
Met	Gln	Asn	Val	Gly	Thr	Ala	Tyr	Ala	Val	Lys	Arg	Ala	Val	Ile	Asp		
		275					280					285					
Gly	Glu	Pro	Ile	Thr	Glu	Arg	Val	Val	Thr	Leu	Thr	Gly	Glu	Ala	Ile		
	290					295					300						

Ala	Arg	Pro	Gly	Asn	Val	Trp	Ala	Arg	Leu	Gly	Thr	Pro	Val	Arg	His
305					310					315					320
Leu	Leu	Asn	Asp	Ala	Gly	Phe	Cys	Pro	Ser	Ala	Asp	Gln	Met	Val	Ile
				325					330						335
Met	Gly	Gly	Pro	Leu	Met	Gly	Phe	Thr	Leu	Pro	Trp	Leu	Asp	Val	Pro
			340					345					350		
Val	Val	Lys	Ile	Thr	Asn	Cys	Leu	Leu	Ala	Pro	Ser	Ala	Asn	Glu	Leu
		355					360					365			
Gly	Glu	Pro	Gln	Glu	Glu	Gln	Ser	Cys	Ile	Arg	Cys	Ser	Ala	Cys	Ala
	370					375					380				
Asp	Ala	Cys	Pro	Ala	Asp	Leu	Leu	Pro	Gln	Gln	Leu	Tyr	Trp	Phe	Ser
385					390					395					400
Lys	Gly	Gln	Gln	His	Asp	Lys	Ala	Thr	Thr	His	Asn	Ile	Ala	Asp	Cys
				405					410					415	
Ile	Glu	Cys	Gly	Ala	Cys	Ala	Trp	Val	Cys	Pro	Ser	Asn	Ile	Pro	Leu
			420					425					430		
Val	Gln	Tyr	Phe	Arg	Gln	Glu	Lys	Ala	Glu	Ile	Ala	Ala	Ile	Arg	Gln
		435					440					445			
Glu	Glu	Lys	Arg	Ala	Ala	Glu	Ala	Lys	Ala	Arg	Phe	Glu	Ala	Arg	Gln
	450					455					460				
Ala	Arg	Leu	Glu	Arg	Glu	Lys	Ala	Ala	Arg	Leu	Glu	Arg	His	Lys	Ser
465					470					475					480
Ala	Ala	Val	Gln	Pro	Ala	Ala	Lys	Asp	Lys	Asp	Ala	Ile	Ala	Ala	Ala
				485					490					495	
Leu	Ala	Arg	Val	Lys	Glu	Lys	Gln	Ala	Gln	Ala	Thr	Gln	Pro	Ile	Val
			500					505					510		
Ile	Lys	Ala	Gly	Glu	Arg	Pro	Asp	Asn	Ser	Ala	Ile	Ile	Ala	Ala	Arg
	515					520						525			
Glu	Ala	Arg	Lys	Ala	Gln	Ala	Arg	Ala	Lys	Gln	Ala	Glu	Leu	Gln	Gln
	530					535				540					
Thr	Asn	Asp	Ala	Ala	Thr	Val	Ala	Asp	Pro	Arg	Lys	Thr	Ala	Val	Glu
545					550					555					560
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Leu	Glu	Gln	Gln	Gln	Ala
				565					570					575	
Asn	Ala	Glu	Pro	Glu	Gln	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Glu
		580						585					590		
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Leu	Glu	Gln	Gln	Gln	Ala
		595				600						605			
Asn	Ala	Glu	Pro	Glu	Glu	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Glu
	610					615				620					
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Leu	Glu	Gln	Gln	Gln	Ala
625					630					635					640
Asn	Ala	Glu	Pro	Glu	Gln	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Glu
			645						650					655	
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Arg	Glu	Gln	Gln	Pro	Ala
			660					665					670		
Asn	Ala	Glu	Pro	Glu	Glu	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Glu
	675						680					685			
Ala	Ala	Ile	Ala	Arg	Ala	Lys	Ala	Arg	Lys	Leu	Glu	Gln	Gln	Gln	Ala
	690					695					700				
Asn	Ala	Val	Pro	Glu	Glu	Gln	Val	Asp	Pro	Arg	Lys	Ala	Ala	Val	Ala
705					710					715					720
Ala	Ala	Ile	Ala	Arg	Ala	Gln	Ala	Lys	Lys	Ala	Ala	Gln	Gln	Lys	Val
				725					730					735	
Val	Asn	Glu	Asp												
			740												

<210> 293
 <211> 352
 <212> PRT
 <213> E. Coli

<400> 293

Met	Val	Phe	Arg	Ile	Ala	Ser	Ser	Pro	Tyr	Thr	His	Asn	Gln	Arg	Gln
1				5					10					15	
Thr	Ser	Arg	Ile	Met	Leu	Leu	Val	Leu	Leu	Ala	Ala	Val	Pro	Gly	Ile
			20					25					30		
Ala	Ala	Gln	Leu	Trp	Phe	Phe	Gly	Trp	Gly	Thr	Leu	Val	Gln	Ile	Leu
		35					40					45			
Leu	Ala	Ser	Val	Ser	Ala	Leu	Leu	Ala	Glu	Ala	Leu	Val	Leu	Lys	Leu
	50					55					60				
Arg	Lys	Gln	Ser	Val	Ala	Ala	Thr	Leu	Lys	Asp	Asn	Ser	Ala	Leu	Leu
65					70					75					80
Thr	Gly	Leu	Leu	Leu	Ala	Val	Ser	Ile	Pro	Pro	Leu	Ala	Pro	Trp	Trp
			85						90					95	
Met	Val	Val	Leu	Gly	Thr	Val	Phe	Ala	Val	Ile	Ile	Ala	Lys	Gln	Leu
			100					105					110		
Tyr	Gly	Gly	Leu	Gly	Gln	Asn	Pro	Phe	Asn	Pro	Ala	Met	Ile	Gly	Tyr
		115				120						125			
Val	Val	Leu	Leu	Ile	Ser	Phe	Pro	Val	Gln	Met	Thr	Ser	Trp	Leu	Pro
	130					135					140				
Pro	His	Glu	Ile	Ala	Val	Asn	Ile	Pro	Gly	Phe	Ile	Asp	Ala	Ile	Gln
145					150					155					160
Val	Ile	Phe	Ser	Gly	His	Thr	Ala	Ser	Gly	Gly	Asp	Met	Asn	Thr	Leu
				165					170					175	
Arg	Leu	Gly	Ile	Asp	Gly	Ile	Ser	Gln	Ala	Thr	Pro	Leu	Asp	Thr	Phe
			180					185					190		
Lys	Thr	Ser	Val	Arg	Ala	Gly	His	Ser	Val	Glu	Gln	Ile	Met	Gln	Tyr
		195					200					205			
Pro	Ile	Tyr	Ser	Gly	Ile	Leu	Ala	Gly	Ala	Gly	Trp	Gln	Trp	Val	Asn
	210					215					220				
Leu	Ala	Trp	Leu	Ala	Gly	Gly	Val	Trp	Leu	Leu	Trp	Gln	Lys	Ala	Ile
225					230					235					240
Arg	Trp	His	Ile	Pro	Leu	Ser	Phe	Leu	Val	Thr	Leu	Ala	Leu	Cys	Ala
				245					250					255	
Met	Leu	Gly	Trp	Leu	Phe	Ser	Pro	Glu	Thr	Leu	Ala	Ala	Pro	Gln	Ile
			260					265					270		
His	Leu	Leu	Ser	Gly	Ala	Thr	Met	Leu	Gly	Ala	Phe	Phe	Ile	Leu	Thr
		275					280					285			
Asp	Pro	Val	Thr	Ala	Ser	Thr	Thr	Asn	Arg	Gly	Arg	Leu	Ile	Phe	Gly
	290					295					300				
Ala	Leu	Ala	Gly	Leu	Leu	Val	Trp	Leu	Ile	Arg	Ser	Phe	Gly	Gly	Tyr
305					310					315					320
Pro	Asp	Gly	Val	Ala	Phe	Ala	Val	Leu	Leu	Ala	Asn	Ile	Thr	Val	Pro
				325					330					335	
Leu	Ile	Asp	Tyr	Tyr	Thr	Arg	Pro	Arg	Val	Tyr	Gly	His	Arg	Lys	Gly
			340					345					350		

<210> 294
 <211> 206
 <212> PRT

<213> E. Coli

<400> 294

Met Leu Lys Thr Ile Arg Lys His Gly Ile Thr Leu Ala Leu Phe Ala
1 5 10 15
Ala Gly Ser Thr Gly Leu Thr Ala Ala Ile Asn Gln Met Thr Lys Thr
20 25 30
Thr Ile Ala Glu Gln Ala Ser Leu Gln Gln Lys Ala Leu Phe Asp Gln
35 40 45
Val Leu Pro Ala Glu Arg Tyr Asn Asn Ala Leu Ala Gln Ser Cys Tyr
50 55 60
Leu Val Thr Ala Pro Glu Leu Gly Lys Gly Glu His Arg Val Tyr Ile
65 70 75 80
Ala Lys Gln Asp Asp Lys Pro Val Ala Ala Val Leu Glu Ala Thr Ala
85 90 95
Pro Asp Gly Tyr Ser Gly Ala Ile Gln Leu Leu Val Gly Ala Asp Phe
100 105 110
Asn Gly Thr Val Leu Gly Thr Arg Val Thr Glu His His Glu Thr Pro
115 120 125
Gly Leu Gly Asp Lys Ile Glu Leu Arg Leu Ser Asp Trp Ile Thr His
130 135 140
Phe Ala Gly Lys Lys Ile Ser Gly Ala Asp Asp Ala His Trp Ala Val
145 150 155 160
Lys Lys Asp Gly Gly Asp Phe Asp Gln Phe Thr Gly Ala Thr Ile Thr
165 170 175
Pro Arg Ala Val Val Asn Ala Val Lys Arg Ala Gly Leu Tyr Ala Gln
180 185 190
Thr Leu Pro Ala Gln Leu Ser Gln Leu Pro Ala Cys Gly Glu
195 200 205

<210> 295

<211> 231

<212> PRT

<213> E. Coli

<400> 295

Met Ser Glu Ile Lys Asp Val Ile Val Gln Gly Leu Trp Lys Asn Asn
1 5 10 15
Ser Ala Leu Val Gln Leu Leu Gly Leu Cys Pro Leu Leu Ala Val Thr
20 25 30
Ser Thr Ala Thr Asn Ala Leu Gly Leu Gly Leu Ala Thr Thr Leu Val
35 40 45
Leu Thr Leu Thr Asn Leu Thr Ile Ser Thr Leu Arg His Trp Thr Pro
50 55 60
Ala Glu Ile Arg Ile Pro Ile Tyr Val Met Ile Ile Ala Ser Val Val
65 70 75 80
Ser Ala Val Gln Met Leu Ile Asn Ala Tyr Ala Phe Gly Leu Tyr Gln
85 90 95
Ser Leu Gly Ile Phe Ile Pro Leu Ile Val Thr Asn Cys Ile Val Val
100 105 110
Gly Arg Ala Glu Ala Phe Ala Ala Lys Lys Gly Pro Ala Leu Ser Ala
115 120 125
Leu Asp Gly Phe Ser Ile Gly Met Gly Ala Thr Cys Ala Met Phe Val
130 135 140
Leu Gly Ser Leu Arg Glu Ile Ile Gly Asn Gly Thr Leu Phe Asp Gly
145 150 155 160

Ala Asp Ala Leu Leu Gly Ser Trp Ala Lys Val Leu Arg Val Glu Ile
 165 170 175
 Phe His Thr Asp Ser Pro Phe Leu Leu Ala Met Leu Pro Pro Gly Ala
 180 185 190
 Phe Ile Gly Leu Gly Leu Met Leu Ala Gly Lys Tyr Leu Ile Asp Glu
 195 200 205
 Arg Met Lys Lys Arg Arg Ala Glu Ala Ala Ala Glu Arg Ala Leu Pro
 210 215 220
 Asn Gly Glu Thr Gly Asn Val
 225 230

<210> 296
 <211> 211
 <212> PRT
 <213> E. Coli

<400> 296
 Met Asn Lys Ala Lys Arg Leu Glu Ile Leu Thr Arg Leu Arg Glu Asn
 1 5 10 15
 Asn Pro His Pro Thr Thr Glu Leu Asn Phe Ser Ser Pro Phe Glu Leu
 20 25 30
 Leu Ile Ala Val Leu Leu Ser Ala Gln Ala Thr Asp Val Ser Val Asn
 35 40 45
 Lys Ala Thr Ala Lys Leu Tyr Pro Val Ala Asn Thr Pro Ala Ala Met
 50 55 60
 Leu Glu Leu Gly Val Glu Gly Val Lys Thr Tyr Ile Lys Thr Ile Gly
 65 70 75 80
 Leu Tyr Asn Ser Lys Ala Glu Asn Ile Ile Lys Thr Cys Arg Ile Leu
 85 90 95
 Leu Glu Gln His Asn Gly Glu Val Pro Glu Asp Arg Ala Ala Leu Glu
 100 105 110
 Ala Leu Pro Gly Val Gly Arg Lys Thr Ala Asn Val Val Leu Asn Thr
 115 120 125
 Ala Phe Gly Trp Pro Thr Ile Ala Val Asp Thr His Ile Phe Arg Val
 130 135 140
 Cys Asn Arg Thr Gln Phe Ala Pro Gly Lys Asn Val Glu Gln Val Glu
 145 150 155 160
 Glu Lys Leu Leu Lys Val Val Pro Ala Glu Phe Lys Val Asp Cys His
 165 170 175
 His Trp Leu Ile Leu His Gly Arg Tyr Thr Cys Ile Ala Arg Lys Pro
 180 185 190
 Arg Cys Gly Ser Cys Ile Ile Glu Asp Leu Cys Glu Tyr Lys Glu Lys
 195 200 205
 Val Asp Ile
 210

<210> 297
 <211> 167
 <212> PRT
 <213> E. Coli

<400> 297
 Met Lys Arg Leu His Lys Arg Phe Leu Leu Ala Thr Phe Cys Ala Leu
 1 5 10 15
 Phe Thr Ala Thr Leu Gln Ala Ala Asp Val Thr Ile Thr Val Asn Gly

002270.012700

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<400> 299
Met Ser Gly Tyr Thr Val Lys Pro Pro Thr Gly Asp Thr Asn Glu Gln
 1      5      10      15
Thr Gln Phe Ile Asp Tyr Phe Asn Leu Phe Tyr Ser Lys Arg Gly Gln
 20      25      30
Glu Gln Ile Ser Ile Ser Gln Gln Leu Gly Asn Tyr Gly Thr Thr Phe
 35      40      45
Phe Ser Ala Ser Arg Gln Ser Tyr Trp Asn Thr Ser Arg Ser Asp Gln
 50      55      60
Gln Ile Ser Phe Gly Leu Asn Val Pro Phe Gly Asp Ile Thr Thr Ser
 65      70      75      80
Leu Asn Tyr Ser Tyr Ser Asn Asn Ile Trp Gln Asn Asp Arg Asp His
 85      90      95
Leu Leu Ala Phe Thr Leu Asn Val Pro Phe Ser His Trp Met Arg Thr
 100     105     110
Asp Ser Gln Ser Ala Phe Arg Asn Ser Asn Ala Ser Tyr Ser Met Ser
 115     120     125
Asn Asp Leu Lys Gly Gly Met Thr Asn Leu Ser Gly Val Tyr Gly Thr
 130     135     140
Leu Leu Pro Asp Asn Asn Leu Asn Tyr Ser Val Gln Val Gly Asn Thr
 145     150     155     160
His Gly Gly Asn Thr Ser Ser Gly Thr Ser Gly Tyr Ser Ser Leu Asn
 165     170     175
Tyr Arg Gly Ala Tyr Gly Asn Thr Asn Val Gly Tyr Ser Arg Ser Gly
 180     185     190
Asp Ser Ser Gln Ile Tyr Tyr Gly Met Ser Gly Gly Ile Ile Ala His
 195     200     205
Ala Asp Gly Ile Thr Phe Gly Gln Pro Leu Gly Asp Thr Met Val Leu
 210     215     220
Val Lys Ala Pro Gly Ala Asp Asn Val Lys Ile Glu Asn Gln Thr Gly
 225     230     235     240
Ile His Thr Asp Trp Arg Gly Tyr Ala Ile Leu Pro Phe Ala Thr Glu
 245     250     255
Tyr Arg Glu Asn Arg Val Ala Leu Asn Ala Asn Ser Leu Ala Asp Asn
 260     265     270
Val Glu Leu Asp Glu Thr Val Val Thr Val Ile Pro Thr His Gly Ala
 275     280     285
Ile Ala Arg Ala Thr Phe Asn Ala Gln Ile Gly Gly Lys Val Leu Met
 290     295     300
Thr Leu Lys Tyr Gly Asn Lys Ser Val Pro Phe Gly Ala Ile Val Thr
 305     310     315     320
His Gly Glu Asn Lys Asn Gly Ser Ile Val Ala Glu Asn Gly Gln Val
 325     330     335
Tyr Leu Thr Gly Leu Pro Gln Ser Gly Gln Leu Gln Val Ser Trp Gly
 340     345     350
Lys Asp Lys Asn Ser Asn Cys Ile Val Glu Tyr Lys Leu Pro Glu Val
 355     360     365
Ser Pro Gly Thr Leu Leu Asn Gln Gln Thr Ala Ile Cys Arg
 370     375     380

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<210> 300
<211> 138
<212> PRT
<213> E. Coli

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<400> 300
 Met Ile Ala Ile Ala Asp Ile Leu Gln Ala Gly Glu Lys Leu Thr Ala
 1 5 10 15
 Val Ala Pro Phe Leu Ala Gly Ile Gln Asn Glu Glu Gln Tyr Thr Gln
 20 25 30
 Ala Leu Glu Leu Val Asp His Leu Leu Leu Asn Asp Pro Glu Asn Pro
 35 40 45
 Leu Leu Asp Leu Val Cys Ala Lys Ile Thr Ala Trp Glu Glu Ser Ala
 50 55 60
 Pro Glu Phe Ala Glu Phe Asn Ala Met Ala Gln Ala Met Pro Gly Gly
 65 70 75 80
 Ile Ala Val Ile Arg Thr Leu Met Asp Gln Tyr Gly Leu Thr Leu Ser
 85 90 95
 Asp Leu Pro Glu Ile Gly Ser Lys Ser Met Val Ser Arg Val Leu Ser
 100 105 110
 Gly Lys Arg Lys Leu Thr Leu Glu His Ala Lys Lys Leu Ala Thr Arg
 115 120 125
 Phe Gly Ile Ser Pro Ala Leu Phe Ile Asp
 130 135

<210> 301
 <211> 104
 <212> PRT
 <213> E. Coli

<400> 301
 Met His Leu Ile Thr Gln Lys Ala Leu Lys Asp Ala Ala Glu Lys Tyr
 1 5 10 15
 Pro Gln His Lys Thr Glu Leu Val Ala Leu Gly Asn Thr Ile Ala Lys
 20 25 30
 Gly Tyr Phe Lys Lys Pro Glu Ser Leu Lys Ala Val Phe Pro Ser Leu
 35 40 45
 Asp Asn Phe Lys Tyr Leu Asp Lys His Tyr Val Phe Asn Val Gly Gly
 50 55 60
 Asn Glu Leu Arg Val Val Ala Met Val Phe Phe Glu Ser Gln Lys Cys
 65 70 75 80
 Tyr Ile Arg Glu Val Met Thr His Lys Glu Tyr Asp Phe Phe Thr Ala
 85 90 95
 Val His Arg Thr Lys Gly Lys Lys
 100

<210> 302
 <211> 2383
 <212> PRT
 <213> E. Coli

<400> 302
 Met Leu Ser Val Phe Thr Phe Phe Arg Cys Ala Arg Lys Gly Ala Phe
 1 5 10 15
 Met Leu Ala Arg Ser Gly Lys Val Ser Met Ala Thr Lys Lys Arg Ser
 20 25 30
 Gly Glu Glu Ile Asn Asp Arg Gln Ile Leu Cys Gly Met Gly Ile Lys
 35 40 45
 Leu Arg Arg Leu Thr Ala Gly Ile Cys Leu Ile Thr Gln Leu Ala Phe

	50					55				60					
Pro 65	Met	Ala	Ala	Ala	Ala	Gln	Gly	Val	Val	Asn	Ala	Ala	Thr	Gln	Gln
Pro	Val	Pro	Ala	Gln	Ile	Ala	Ile	Ala	Asn	Ala	Asn	Thr	Val	Pro	Tyr
Thr	Leu	Gly	Ala	Leu	Glu	Ser	Ala	Gln	Ser	Val	Ala	Glu	Arg	Phe	Gly
Ile	Ser	Val	Ala	Glu	Leu	Arg	Lys	Leu	Asn	Gln	Phe	Arg	Thr	Phe	Ala
Arg	Ser	Phe	Asp	Asn	Val	Arg	Gln	Gly	Asp	Glu	Leu	Asp	Val	Pro	Ala
Gln 145	Val	Ser	Glu	Lys	Lys	Leu	Thr	Pro	Pro	Pro	Gly	Asn	Ser	Ser	Asp
Asn	Leu	Glu	Gln	Gln	Ile	Ala	Ser	Thr	Ser	Gln	Gln	Ile	Gly	Ser	Leu
Leu	Ala	Glu	Asp	Met	Asn	Ser	Glu	Gln	Ala	Ala	Asn	Met	Ala	Arg	Gly
Trp	Ala	Ser	Ser	Gln	Ala	Ser	Gly	Ala	Met	Thr	Asp	Trp	Leu	Ser	Arg
Phe	Gly	Thr	Ala	Arg	Ile	Thr	Leu	Gly	Val	Asp	Glu	Asp	Phe	Ser	Leu
Lys 225	Asn	Ser	Gln	Phe	Asp	Phe	Leu	His	Pro	Trp	Tyr	Glu	Thr	Pro	Asp
Asn	Leu	Phe	Phe	Ser	Gln	His	Thr	Leu	His	Arg	Thr	Asp	Glu	Arg	Thr
Gln	Ile	Asn	Asn	Gly	Leu	Gly	Trp	Arg	His	Phe	Thr	Pro	Thr	Trp	Met
Ser	Gly	Ile	Asn	Phe	Phe	Phe	Asp	His	Asp	Leu	Ser	Arg	Tyr	His	Ser
Arg	Ala	Gly	Ile	Gly	Ala	Glu	Tyr	Trp	Arg	Asp	Tyr	Leu	Lys	Leu	Ser
Ser 305	Asn	Gly	Tyr	Leu	Arg	Leu	Thr	Asn	Trp	Arg	Ser	Ala	Pro	Glu	Leu
Asp	Asn	Asp	Tyr	Glu	Ala	Arg	Pro	Ala	Asn	Gly	Trp	Asp	Val	Arg	Ala
Glu	Ser	Trp	Leu	Pro	Ala	Trp	Pro	His	Leu	Gly	Gly	Lys	Leu	Val	Tyr
Glu	Gln	Tyr	Tyr	Gly	Asp	Glu	Val	Ala	Leu	Phe	Asp	Lys	Asp	Asp	Arg
Gln	Ser	Asn	Pro	His	Ala	Ile	Thr	Ala	Gly	Leu	Asn	Tyr	Thr	Pro	Phe
Pro 385	Leu	Met	Thr	Phe	Ser	Ala	Glu	Gln	Arg	Gln	Gly	Lys	Gln	Gly	Glu
Asn	Asp	Thr	Arg	Phe	Ala	Val	Asp	Phe	Thr	Trp	Gln	Pro	Gly	Ser	Ala
Met	Gln	Lys	Gln	Leu	Asp	Pro	Asn	Glu	Val	Ala	Ala	Arg	Arg	Ser	Leu
Ala	Gly	Ser	Arg	Tyr	Asp	Leu	Val	Asp	Arg	Asn	Asn	Asn	Ile	Val	Leu
Glu	Tyr	Arg	Lys	Lys	Glu	Leu	Val	Arg	Leu	Thr	Leu	Thr	Asp	Pro	Val
Thr 465	Gly	Lys	Ser	Gly	Glu	Val	Lys	Ser	Leu	Val	Ser	Ser	Leu	Gln	Thr
Lys	Tyr	Ala	Leu	Lys	Gly	Tyr	Asn	Val	Glu	Ala	Thr	Ala	Leu	Glu	Ala
Ala	Gly	Gly	Lys	Val	Val	Thr	Thr	Gly	Lys	Asp	Ile	Leu	Val	Thr	Leu

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Pro	Ala	Tyr	Arg	Phe	Thr	Ser	Thr	Pro	Glu	Thr	Asp	Asn	Thr	Trp	Pro
		515					520					525			
Ile	Glu	Val	Thr	Ala	Glu	Asp	Val	Lys	Gly	Asn	Leu	Ser	Asn	Arg	Glu
		530				535					540				
Gln	Ser	Met	Val	Val	Val	Gln	Ala	Pro	Thr	Leu	Ser	Gln	Lys	Asp	Ser
545					550					555					560
Ser	Val	Ser	Leu	Ser	Thr	Gln	Thr	Leu	Asn	Ala	Asp	Ser	His	Ser	Thr
				565					570					575	
Ala	Thr	Leu	Thr	Phe	Ile	Ala	His	Asp	Ala	Ala	Gly	Asn	Pro	Val	Val
			580					585					590		
Gly	Leu	Val	Leu	Ser	Thr	Arg	His	Glu	Gly	Val	Gln	Asp	Ile	Thr	Leu
		595				600						605			
Ser	Asp	Trp	Lys	Asp	Asn	Gly	Asp	Gly	Ser	Tyr	Thr	Gln	Ile	Leu	Thr
	610					615					620				
Thr	Gly	Ala	Met	Ser	Gly	Thr	Leu	Thr	Leu	Met	Pro	Gln	Leu	Asn	Gly
625					630					635					640
Val	Asp	Ala	Ala	Lys	Ala	Pro	Ala	Val	Val	Asn	Ile	Ile	Ser	Val	Ser
				645					650					655	
Ser	Ser	Arg	Thr	His	Ser	Ser	Ile	Lys	Ile	Asp	Lys	Asp	Arg	Tyr	Leu
			660					665					670		
Ser	Gly	Asn	Pro	Ile	Glu	Val	Thr	Val	Glu	Leu	Arg	Asp	Glu	Asn	Asp
		675					680					685			
Lys	Pro	Val	Lys	Glu	Gln	Lys	Gln	Gln	Leu	Asn	Asn	Ala	Val	Ser	Ile
	690					695					700				
Asp	Asn	Val	Lys	Pro	Gly	Val	Thr	Thr	Asp	Trp	Lys	Glu	Thr	Ala	Asp
705					710					715					720
Gly	Val	Tyr	Lys	Ala	Thr	Tyr	Thr	Ala	Tyr	Thr	Lys	Gly	Ser	Gly	Leu
				725					730					735	
Thr	Ala	Lys	Leu	Met	Gln	Asn	Trp	Asn	Glu	Asp	Leu	His	Thr	Ala	
			740				745					750			
Gly	Phe	Ile	Ile	Asp	Ala	Asn	Pro	Gln	Ser	Ala	Lys	Ile	Ala	Thr	Leu
		755					760					765			
Ser	Ala	Ser	Asn	Asn	Gly	Val	Leu	Ala	Asn	Glu	Asn	Ala	Ala	Asn	Thr
	770					775					780				
Val	Ser	Val	Asn	Val	Ala	Asp	Glu	Gly	Ser	Asn	Pro	Ile	Asn	Asp	His
785					790					795					800
Thr	Val	Thr	Phe	Ala	Val	Leu	Ser	Gly	Ser	Ala	Thr	Ser	Phe	Asn	Asn
			805					810						815	
Gln	Asn	Thr	Ala	Lys	Thr	Asp	Val	Asn	Gly	Leu	Ala	Thr	Phe	Asp	Leu
			820					825					830		
Lys	Ser	Ser	Lys	Gln	Glu	Asp	Asn	Thr	Val	Glu	Val	Thr	Leu	Glu	Asn
		835					840					845			
Gly	Val	Lys	Gln	Thr	Leu	Ile	Val	Ser	Phe	Val	Gly	Asp	Ser	Ser	Thr
	850					855					860				
Ala	Gln	Val	Asp	Leu	Gln	Lys	Ser	Lys	Asn	Glu	Val	Val	Ala	Asp	Gly
865					870					875					880
Asn	Asp	Ser	Val	Thr	Met	Thr	Ala	Thr	Val	Arg	Asp	Ala	Lys	Gly	Asn
				885					890					895	
Leu	Leu	Asn	Asp	Val	Met	Val	Thr	Phe	Asn	Val	Asn	Ser	Ala	Glu	Ala
			900					905					910		
Lys	Leu	Ser	Gln	Thr	Glu	Val	Asn	Ser	His	Asp	Gly	Ile	Ala	Thr	Ala
		915					920					925			
Thr	Leu	Thr	Ser	Leu	Lys	Asn	Gly	Asp	Tyr	Arg	Val	Thr	Ala	Ser	Val
	930					935					940				
Ser	Ser	Gly	Ser	Gln	Ala	Asn	Gln	Gln	Val	Asn	Phe	Ile	Gly	Asp	Gln
945					950					955					960
Ser	Thr	Ala	Ala	Leu	Thr	Leu	Ser	Val	Pro	Ser	Gly	Asp	Ile	Thr	Val

[illegible]

Pro Ser Glu Gly Val Thr Pro Ser Asn Asn Ala Ile Tyr Thr Thr Asn
 1425 1430 1435 1440
 His Asp Gly Asn Phe Tyr Ala Ser Phe Thr Ala Thr Lys Ala Gly Val
 1445 1450 1455
 Tyr Gln Leu Thr Ala Thr Leu Glu Asn Gly Asp Ser Met Gln Gln Thr
 1460 1465 1470
 Val Thr Tyr Val Pro Asn Val Ala Asn Ala Glu Ile Thr Leu Ala Ala
 1475 1480 1485
 Ser Lys Asp Pro Val Ile Ala Asp Asn Asn Asp Leu Thr Thr Leu Thr
 1490 1495 1500
 Ala Thr Val Ala Asp Thr Glu Gly Asn Ala Ile Ala Asn Thr Glu Val
 1505 1510 1515 1520
 Thr Phe Thr Leu Pro Glu Asp Val Lys Ala Asn Phe Thr Leu Ser Asp
 1525 1530 1535
 Gly Gly Lys Val Ile Thr Asp Ala Glu Gly Lys Ala Lys Val Thr Leu
 1540 1545 1550
 Lys Gly Thr Lys Ala Gly Ala His Thr Val Thr Ala Ser Met Thr Gly
 1555 1560 1565
 Gly Lys Ser Glu Gln Leu Val Val Asn Phe Ile Ala Asp Thr Leu Thr
 1570 1575 1580
 Ala Gln Val Asn Leu Asn Val Thr Glu Asp Asn Phe Ile Ala Asn Asn
 1585 1590 1595 1600
 Val Gly Met Thr Arg Leu Gln Ala Thr Val Thr Asp Gly Asn Gly Asn
 1605 1610 1615
 Pro Leu Ala Asn Glu Ala Val Thr Phe Thr Leu Pro Ala Asp Val Ser
 1620 1625 1630
 Ala Ser Phe Thr Leu Gly Gln Gly Gly Ser Ala Ile Thr Asp Ile Asn
 1635 1640 1645
 Gly Lys Ala Glu Val Thr Leu Ser Gly Thr Lys Ser Gly Thr Tyr Pro
 1650 1655 1660
 Val Thr Val Ser Val Asn Asn Tyr Gly Val Ser Asp Thr Lys Gln Val
 1665 1670 1675 1680
 Thr Leu Ile Ala Asp Ala Gly Thr Ala Lys Leu Ala Ser Leu Thr Ser
 1685 1690 1695
 Val Tyr Ser Phe Val Val Ser Thr Thr Glu Gly Ala Thr Met Thr Ala
 1700 1705 1710
 Ser Val Thr Asp Ala Asn Gly Asn Pro Val Glu Gly Ile Lys Val Asn
 1715 1720 1725
 Phe Arg Gly Thr Ser Val Thr Leu Ser Ser Thr Ser Val Glu Thr Asp
 1730 1735 1740
 Asp Arg Gly Phe Ala Glu Ile Leu Val Thr Ser Thr Glu Val Gly Leu
 1745 1750 1755 1760
 Lys Thr Val Ser Ala Ser Leu Ala Asp Lys Pro Thr Glu Val Ile Ser
 1765 1770 1775
 Arg Leu Leu Asn Ala Ser Ala Asp Val Asn Ser Ala Thr Ile Thr Ser
 1780 1785 1790
 Leu Glu Ile Pro Glu Gly Gln Val Met Val Ala Gln Asp Val Ala Val
 1795 1800 1805
 Lys Ala His Val Asn Asp Gln Phe Gly Asn Pro Val Ala His Gln Pro
 1810 1815 1820
 Val Thr Phe Ser Ala Glu Pro Ser Ser Gln Met Ile Ile Ser Gln Asn
 1825 1830 1835 1840
 Thr Val Ser Thr Asn Thr Gln Gly Val Ala Glu Val Thr Met Thr Pro
 1845 1850 1855
 Glu Arg Asn Gly Ser Tyr Met Val Lys Ala Ser Leu Pro Asn Gly Ala
 1860 1865 1870
 Ser Leu Glu Lys Gln Leu Glu Ala Ile Asp Glu Lys Leu Thr Leu Thr

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1875	1880	1885
Ala Ser Ser Pro Leu Ile Gly Val Tyr Ala Pro Thr Gly Ala Thr Leu		
1890	1895	1900
Thr Ala Thr Leu Thr Ser Ala Asn Gly Thr Pro Val Glu Gly Gln Val		
1905	1910	1915
Ile Asn Phe Ser Val Thr Pro Glu Gly Ala Thr Leu Ser Gly Gly Lys		1920
1925	1930	1935
Val Arg Thr Asn Ser Ser Gly Gln Ala Pro Val Val Leu Thr Ser Asn		
1940	1945	1950
Lys Val Gly Thr Tyr Thr Val Thr Ala Ser Phe His Asn Gly Val Thr		
1955	1960	1965
Ile Gln Thr Gln Thr Thr Val Lys Val Thr Gly Asn Ser Ser Thr Ala		
1970	1975	1980
His Val Ala Ser Phe Ile Ala Asp Pro Ser Thr Ile Ala Ala Thr Asn		
1985	1990	1995
Thr Asp Leu Ser Thr Leu Lys Ala Thr Val Glu Asp Gly Ser Gly Asn		2000
2005	2010	2015
Leu Ile Glu Gly Leu Thr Val Tyr Phe Ala Leu Lys Ser Gly Ser Ala		
2020	2025	2030
Thr Leu Thr Ser Leu Thr Ala Val Thr Asp Gln Asn Gly Ile Ala Thr		
2035	2040	2045
Thr Ser Val Lys Gly Ala Met Thr Gly Ser Val Thr Val Ser Ala Val		
2050	2055	2060
Thr Thr Ala Gly Gly Met Gln Thr Val Asp Ile Thr Leu Val Ala Gly		
2065	2070	2075
Pro Ala Asp Thr Ser Gln Ser Val Leu Lys Ser Asn Arg Ser Ser Leu		
2085	2090	2095
Lys Gly Asp Tyr Thr Asp Ser Ala Glu Leu Arg Leu Val Leu His Asp		
2100	2105	2110
Ile Ser Gly Asn Pro Ile Lys Val Ser Glu Gly Met Glu Phe Val Gln		
2115	2120	2125
Ser Gly Thr Asn Val Pro Tyr Ile Lys Ile Ser Ala Ile Asp Tyr Ser		
2130	2135	2140
Leu Asn Ile Asn Gly Asp Tyr Lys Ala Thr Val Thr Gly Gly Gly Glu		
2145	2150	2155
Gly Ile Ala Thr Leu Ile Pro Val Leu Asn Gly Val His Gln Ala Gly		
2165	2170	2175
Leu Ser Thr Thr Ile Gln Phe Thr Arg Ala Glu Asp Lys Ile Met Ser		
2180	2185	2190
Gly Thr Val Ser Val Asn Gly Thr Asp Leu Pro Thr Thr Thr Phe Pro		
2195	2200	2205
Ser Gln Gly Phe Thr Gly Ala Tyr Tyr Gln Leu Asn Asn Asp Asn Phe		
2210	2215	2220
Ala Pro Gly Lys Thr Ala Ala Asp Tyr Glu Phe Ser Ser Ser Ala Ser		
2225	2230	2235
Trp Val Asp Val Asp Ala Thr Gly Lys Val Thr Phe Lys Asn Val Gly		
2245	2250	2255
Ser Asn Ser Glu Arg Ile Thr Ala Thr Pro Lys Ser Gly Gly Pro Ser		
2260	2265	2270
Tyr Val Tyr Glu Ile Arg Val Lys Ser Trp Trp Val Asn Ala Gly Glu		
2275	2280	2285
Ala Phe Met Ile Tyr Ser Leu Ala Glu Asn Phe Cys Ser Ser Asn Gly		
2290	2295	2300
Tyr Thr Leu Pro Arg Ala Asn Tyr Leu Asn His Cys Ser Ser Arg Gly		
2305	2310	2315
Ile Gly Ser Leu Tyr Ser Glu Trp Gly Asp Met Gly His Tyr Thr Thr		
2325	2330	2335

Asp Ala Gly Phe Gln Ser Asn Met Tyr Trp Ser Ser Ser Pro Ala Asn
 2340 2345 2350
 Ser Ser Glu Gln Tyr Val Val Ser Leu Ala Thr Gly Asp Gln Ser Val
 2355 2360 2365
 Phe Glu Lys Leu Gly Phe Ala Tyr Ala Thr Cys Tyr Lys Asn Leu
 2370 2375 2380

<210> 303
 <211> 61
 <212> PRT
 <213> E. Coli

<400> 303
 Met Ser Lys Gly Ala Leu Tyr Glu Phe Asn Asn Pro Asp Gln Leu Lys
 1 5 10 15
 Ile Pro Leu Pro His Lys His Ile Ala Ser Thr Phe Asn Asp Ile Met
 20 25 30
 Ser Lys Asp Val Gly Tyr Ala Tyr Val Ser Leu Leu Tyr Ala Cys Pro
 35 40 45
 Leu Lys Thr His Ser Leu Arg Leu Asn Pro Phe Ser Lys
 50 55 60

<210> 304
 <211> 398
 <212> PRT
 <213> E. Coli

<400> 304
 Met Gln Val Ala Glu Gln Arg Ile Gln Leu Ala Glu Ala Gln Ala Lys
 1 5 10 15
 Ala Val Ala Thr Gln Asp Gly Pro Gln Ile Asp Phe Ser Ala Asp Met
 20 25 30
 Glu Arg Gln Lys Met Ser Ala Glu Gly Leu Met Gly Pro Phe Ala Leu
 35 40 45
 Asn Asp Pro Ala Ala Gly Thr Thr Gly Pro Trp Tyr Thr Asn Gly Thr
 50 55 60
 Phe Gly Leu Thr Ala Gly Trp His Leu Asp Ile Trp Gly Lys Asn Arg
 65 70 75 80
 Ala Glu Val Thr Ala Arg Leu Gly Thr Val Lys Ala Arg Ala Ala Glu
 85 90 95
 Arg Glu Gln Thr Arg Gln Leu Leu Ala Gly Ser Val Ala Arg Leu Tyr
 100 105 110
 Trp Glu Trp Gln Thr Gln Ala Ala Leu Asn Thr Val Leu Gln Gln Ile
 115 120 125
 Glu Lys Glu Gln Asn Thr Ile Ile Ala Thr Asp Arg Gln Leu Tyr Gln
 130 135 140
 Asn Gly Ile Thr Ser Ser Val Glu Gly Val Glu Thr Asp Ile Asn Ala
 145 150 155 160
 Ser Lys Thr Arg Gln Gln Leu Asn Asp Val Ala Gly Lys Met Lys Ile
 165 170 175
 Ile Glu Ala Arg Leu Ser Ala Leu Thr Asn Asn Gln Thr Lys Ser Leu
 180 185 190
 Lys Leu Lys Pro Val Ala Leu Pro Lys Val Ala Ser Gln Leu Pro Asp
 195 200 205
 Glu Leu Gly Tyr Ser Leu Leu Ala Arg Arg Ala Asp Leu Gln Ala Ala

210	215	220
His Trp Tyr Val Glu Ser Ser Leu Ser Thr Ile Asp Ala Ala Lys Ala		
225	230	235
Ala Phe Tyr Pro Asp Ile Asn Leu Met Ala Phe Leu Gln Gln Asp Ala		240
	245	250
Leu His Leu Ser Asp Leu Phe Arg His Ser Ala Gln Gln Met Gly Val		255
	260	265
Thr Ala Gly Leu Thr Leu Pro Ile Phe Asp Ser Gly Arg Leu Asn Ala		270
	275	280
Asn Leu Asp Ile Ala Lys Ala Glu Ser Asn Leu Ser Ile Ala Ser Tyr		285
	290	295
Asn Lys Ala Val Val Glu Ala Val Asn Asp Val Ala Arg Ala Ala Ser		300
305	310	315
Gln Val Gln Thr Leu Ala Glu Lys Asn Gln His Gln Ala Gln Ile Glu		320
	325	330
Arg Asp Ala Leu Arg Val Val Gly Leu Ala Gln Ala Arg Phe Asn Ala		335
	340	345
Gly Ile Ile Ala Gly Ser Arg Val Ser Glu Ala Arg Ile Pro Ala Leu		350
	355	360
Arg Glu Arg Ala Asn Gly Leu Leu Leu Gln Gly Gln Trp Leu Asp Ala		365
	370	375
Ser Ile Gln Leu Thr Gly Ala Leu Gly Gly Gly Tyr Lys Arg		380
385	390	395

<210> 305
 <211> 96
 <212> PRT
 <213> E. Coli

<400> 305

Met Tyr Cys His Ala Lys Leu Lys Asn Ile Ser Gln His Thr Val Ile	
1	5
Ser Ala His Leu Phe Leu Pro Asp Tyr Ser Pro Met Asn Arg Asp Ser	
	20
Phe Tyr Pro Ala Ile Ala Cys Phe Pro Leu Leu Leu Met Leu Ala Gly	
	35
Cys Ala Pro Met His Glu Thr Arg Gln Ala Leu Ser Gln Gln Thr Pro	
	50
Ala Ala Gln Val Asp Thr Ala Leu Pro Thr Ala Leu Lys Met Val Gly	
65	70
Gln Thr Ala Asn Gly Gly Trp Ser Ile Thr Ile Ile Asn Ser Leu Pro	
	85
	90
	95

<210> 306
 <211> 315
 <212> PRT
 <213> E. Coli

<400> 306

Met Arg Val Leu Leu Ala Pro Met Glu Gly Val Leu Asp Ser Leu Val	
1	5
Arg Glu Leu Leu Thr Glu Val Asn Asp Tyr Asp Leu Cys Ile Thr Glu	
	20
Phe Val Arg Val Val Asp Gln Leu Leu Pro Val Lys Val Phe His Arg	
	35
	40
	45

Ile Cys Pro Glu Leu Gln Asn Ala Ser Arg Thr Pro Ser Gly Thr Leu
 50 55 60
 Val Arg Val Gln Leu Leu Gly Gln Phe Pro Gln Trp Leu Ala Glu Asn
 65 70 75 80
 Ala Ala Arg Ala Val Glu Leu Gly Ser Trp Gly Val Asp Leu Asn Cys
 85 90 95
 Gly Cys Pro Ser Lys Thr Val Asn Gly Ser Gly Gly Gly Ala Thr Leu
 100 105 110
 Leu Lys Asp Pro Glu Leu Ile Tyr Gln Gly Ala Lys Ala Met Arg Glu
 115 120 125
 Ala Val Pro Ala His Leu Pro Val Ser Val Lys Val Arg Leu Gly Trp
 130 135 140
 Asp Ser Gly Glu Lys Lys Phe Glu Ile Ala Asp Ala Val Gln Gln Ala
 145 150 155 160
 Gly Ala Thr Glu Leu Val Val His Gly Arg Thr Lys Glu Gln Gly Tyr
 165 170 175
 Arg Ala Glu His Ile Asp Trp Gln Ala Ile Gly Asp Ile Arg Gln Arg
 180 185 190
 Leu Asn Ile Pro Val Ile Ala Asn Gly Glu Ile Trp Asp Trp Gln Ser
 195 200 205
 Ala Gln Gln Cys Met Ala Ile Ser Gly Cys Asp Ala Val Met Ile Gly
 210 215 220
 Arg Gly Ala Leu Asn Ile Pro Asn Leu Ser Arg Val Val Lys Tyr Asn
 225 230 235 240
 Glu Pro Arg Met Pro Trp Pro Glu Val Val Ala Leu Leu Gln Lys Tyr
 245 250 255
 Thr Arg Leu Glu Lys Gln Gly Asp Thr Gly Leu Tyr His Val Ala Arg
 260 265 270
 Ile Lys Gln Trp Leu Ser Tyr Leu Arg Lys Glu Tyr Asp Glu Ala Thr
 275 280 285
 Glu Leu Phe Gln His Val Arg Val Leu Asn Asn Ser Pro Asp Ile Ala
 290 295 300
 Arg Ala Ile Gln Ala Ile Asp Ile Glu Lys Leu
 305 310 315

<210> 307
 <211> 296
 <212> PRT
 <213> E. Coli

<400> 307
 Met Thr Ile Ser Thr Thr Ser Thr Pro His Asp Ala Val Phe Lys Ser
 1 5 10 15
 Phe Leu Arg His Pro Asp Thr Ala Arg Asp Phe Ile Asp Ile His Leu
 20 25 30
 Pro Ala Pro Leu Arg Lys Leu Cys Asp Leu Thr Thr Leu Lys Leu Glu
 35 40 45
 Pro Asn Ser Phe Ile Asp Glu Asp Leu Arg Gln Tyr Tyr Ser Asp Leu
 50 55 60
 Leu Trp Ser Val Lys Thr Gln Glu Gly Val Gly Tyr Ile Tyr Val Val
 65 70 75 80
 Ile Glu His Gln Ser Lys Pro Glu Glu Leu Met Ala Phe Arg Met Met
 85 90 95
 Arg Tyr Ser Ile Ala Ala Met Gln Asn His Leu Asp Ala Gly Tyr Lys
 100 105 110
 Glu Leu Pro Leu Val Leu Pro Met Leu Phe Tyr His Gly Cys Arg Ser

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      115              120              125
Pro Tyr Pro Tyr Ser Leu Cys Trp Leu Asp Glu Phe Ala Glu Pro Ala
 130              135              140
Ile Ala Arg Lys Ile Tyr Ser Ser Ala Phe Pro Leu Val Asp Ile Thr
 145              150              155              160
Val Val Pro Asp Asp Glu Ile Met Gln His Arg Lys Met Ala Leu Leu
      165              170              175
Glu Leu Ile Gln Lys His Ile Arg Gln Arg Asp Leu Leu Gly Leu Val
      180              185              190
Asp Gln Ile Val Ser Leu Leu Val Thr Gly Asn Thr Asn Asp Arg Gln
      195              200              205
Leu Lys Ala Leu Phe Asn Tyr Val Leu Gln Thr Gly Asp Ala Gln Arg
      210              215              220
Phe Arg Ala Phe Ile Gly Glu Ile Ala Glu Arg Ala Pro Gln Glu Lys
 225              230              235              240
Glu Lys Leu Met Thr Ile Ala Asp Arg Leu Arg Glu Glu Gly Ala Met
      245              250              255
Gln Gly Lys His Glu Glu Ala Leu Arg Ile Ala Gln Glu Met Leu Asp
      260              265              270
Arg Gly Leu Asp Arg Glu Leu Val Met Met Val Thr Arg Leu Ser Pro
      275              280              285
Asp Asp Leu Ile Ala Gln Ser His
      290              295

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<210> 308
 <211> 555
 <212> PRT
 <213> E. Coli

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      <400> 308
<400> 3
Met Ala Gln Phe Val Tyr Thr Met His Arg Val Gly Lys Val Val Pro
 1              5              10              15
Pro Lys Arg His Ile Leu Lys Asn Ile Ser Leu Ser Phe Phe Pro Gly
      20              25              30
Ala Lys Ile Gly Val Leu Gly Leu Asn Gly Ala Gly Lys Ser Thr Leu
      35              40              45
Leu Arg Ile Met Ala Gly Ile Asp Lys Asp Ile Glu Gly Glu Ala Arg
      50              55              60
Pro Gln Pro Asp Ile Lys Ile Gly Tyr Leu Pro Gln Glu Pro Gln Leu
 65              70              75              80
Asn Pro Glu His Thr Val Arg Glu Ser Ile Glu Glu Ala Val Ser Glu
      85              90              95
Val Val Asn Ala Leu Lys Arg Leu Asp Glu Val Tyr Ala Leu Tyr Ala
      100              105              110
Asp Pro Asp Ala Asp Phe Asp Lys Leu Ala Ala Glu Gln Gly Arg Leu
      115              120              125
Glu Glu Ile Ile Gln Ala His Asp Gly His Asn Leu Asn Val Gln Leu
      130              135              140
Glu Arg Ala Ala Asp Ala Leu Arg Leu Pro Asp Trp Asp Ala Lys Ile
 145              150              155              160
Ala Asn Leu Ser Gly Gly Glu Arg Arg Arg Val Ala Leu Cys Arg Leu
      165              170              175
Leu Leu Glu Lys Pro Asp Met Leu Leu Leu Asp Glu Pro Thr Asn His
      180              185              190
Leu Asp Ala Glu Ser Val Ala Trp Leu Glu Arg Phe Leu His Asp Phe

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Glu	Gly	Thr	Val	Val	Ala	Ile	Thr	His	Asp	Arg	Tyr	Phe	Leu	Asp	Asn
	210					215					220				
Val	Ala	Gly	Trp	Ile	Leu	Glu	Leu	Asp	Arg	Gly	Glu	Gly	Ile	Pro	Trp
225					230					235					240
Glu	Gly	Asn	Tyr	Ser	Ser	Trp	Leu	Glu	Gln	Lys	Asp	Gln	Arg	Leu	Ala
				245					250					255	
Gln	Glu	Ala	Ser	Gln	Glu	Ala	Ala	Arg	Arg	Lys	Ser	Ile	Glu	Lys	Glu
			260					265					270		
Leu	Glu	Trp	Val	Arg	Gln	Gly	Thr	Lys	Gly	Arg	Gln	Ser	Lys	Gly	Lys
		275					280					285			
Ala	Arg	Leu	Ala	Arg	Phe	Glu	Glu	Leu	Asn	Ser	Thr	Glu	Tyr	Gln	Lys
	290					295					300				
Arg	Asn	Glu	Thr	Asn	Glu	Leu	Phe	Ile	Pro	Pro	Gly	Pro	Arg	Leu	Gly
305					310					315					320
Asp	Lys	Val	Leu	Glu	Val	Ser	Asn	Leu	Arg	Lys	Ser	Tyr	Gly	Asp	Arg
				325					330					335	
Leu	Leu	Ile	Asp	Asp	Leu	Ser	Phe	Ser	Ile	Pro	Lys	Gly	Ala	Ile	Val
			340					345					350		
Gly	Ile	Ile	Gly	Pro	Asn	Gly	Ala	Gly	Lys	Ser	Thr	Leu	Phe	Arg	Met
		355					360					365			
Ile	Ser	Gly	Gln	Glu	Gln	Pro	Asp	Ser	Gly	Thr	Ile	Thr	Leu	Gly	Glu
	370					375					380				
Thr	Val	Lys	Leu	Ala	Ser	Val	Asp	Gln	Phe	Arg	Asp	Ser	Met	Asp	Asn
385					390					395					400
Ser	Lys	Thr	Val	Trp	Glu	Glu	Val	Ser	Gly	Gly	Leu	Asp	Ile	Met	Lys
				405					410					415	
Ile	Gly	Asn	Thr	Glu	Met	Pro	Ser	Arg	Ala	Tyr	Val	Gly	Arg	Phe	Asn
			420					425					430		
Phe	Lys	Gly	Val	Asp	Gln	Gly	Lys	Arg	Val	Gly	Glu	Leu	Ser	Gly	Gly
		435					440					445			
Glu	Arg	Gly	Arg	Leu	His	Leu	Ala	Lys	Leu	Leu	Gln	Val	Gly	Gly	Asn
						455					460				
Met	Leu	Leu	Leu	Asp	Glu	Pro	Thr	Asn	Asp	Leu	Asp	Ile	Glu	Thr	Leu
465					470					475					480
Arg	Ala	Leu	Glu	Asn	Ala	Leu	Leu	Glu	Phe	Pro	Gly	Cys	Ala	Met	Val
				485					490					495	
Ile	Ser	His	Asp	Arg	Trp	Phe	Leu	Asp	Arg	Ile	Ala	Thr	His	Ile	Leu
			500					505					510		
Asp	Tyr	Gln	Asp	Glu	Gly	Lys	Val	Glu	Phe	Phe	Glu	Gly	Asn	Phe	Thr
		515					520					525			
Glu	Tyr	Glu	Glu	Tyr	Lys	Lys	Arg	Thr	Leu	Gly	Ala	Asp	Ala	Leu	Glu
		530				535					540				
Pro	Lys	Arg	Ile	Lys	Tyr	Lys	Arg	Ile	Ala	Lys					
545					550										

<210> 309
<211> 173
<212> PRT
<213> E. Coli

<400> 309
Met Ser Lys Pro Lys Tyr Pro Phe Glu Lys Arg Leu Glu Val Val Asn
1 5 10 15
His Tyr Phe Thr Thr Asp Asp Gly Tyr Arg Ile Ile Ser Ala Arg Phe

Figure 1 consists of 12 bar charts, labeled (a) through (l), each representing a different demographic or attitudinal variable. Each chart compares two groups: 'No. of respondents' (white bars) and 'No. of respondents' (black bars). The x-axis for all charts is 'Percentage of respondents' ranging from 0 to 100. The y-axis for all charts is 'No. of respondents' ranging from 0 to 100.

- (a) Age: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (b) Sex: The white bar is at approximately 55% and the black bar is at approximately 45%.
- (c) Education: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (d) Income: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (e) Employment: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (f) Home ownership: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (g) Marital status: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (h) Religion: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (i) Political affiliation: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (j) Attitude towards gay/lesbian: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (k) Attitude towards transgender: The white bar is at approximately 65% and the black bar is at approximately 35%.
- (l) Attitude towards HIV/AIDS: The white bar is at approximately 65% and the black bar is at approximately 35%.

<211> 38

<213> E.

[illegible]

<211> 443

<213> E.

Met 1	Ala	Lys	Gln	Pro 5	Gly	Leu	Asp	Phe	Gln 10	Ser	Ala	Lys	Gly 15	Gly	Leu
Gly	Glu	Leu	Lys 20	Arg	Arg	Leu	Leu	Phe 25	Val	Ile	Gly	Ala	Leu 30	Ile	Val
Phe	Arg	Ile 35	Gly	Ser	Phe	Ile	Pro 40	Ile	Pro	Gly	Ile	Asp 45	Ala	Ala	Val
Leu	Ala 50	Lys	Leu	Leu	Glu	Gln 55	Gln	Arg	Gly	Thr	Ile	Ile 60	Glu	Met	Phe
Asn 65	Met	Phe	Ser	Gly	Gly 70	Ala	Leu	Ser	Arg	Ala 75	Ser	Ile 80	Phe	Ala	Leu
Gly	Ile	Met	Pro	Tyr 85	Ile	Ser	Ala	Ser	Ile 90	Ile	Ile	Gln 95	Leu	Leu	Thr
Val	Val	His	Pro 100	Thr	Leu	Ala	Glu	Ile 105	Lys	Lys	Glu	Gly 110	Glu	Ser	Gly
Arg	Arg	Lys 115	Ile	Ser	Gln	Tyr	Thr 120	Arg	Tyr	Gly	Thr	Leu 125	Val	Leu	Ala
Ile	Phe 130	Gln	Ser	Ile	Gly	Ile 135	Ala	Thr	Gly	Leu	Pro 140	Asn 145	Met	Pro	Gly
Met 145	Gln	Gly	Leu	Val 150	Ile	Asn	Pro	Gly	Phe 155	Ala	Phe	Tyr 160	Phe	Thr	Ala
Val	Val	Ser	Leu	Val 165	Thr	Gly	Thr	Met	Phe 170	Leu	Met	Trp 175	Leu	Gly	Glu
Gln	Ile	Thr	Glu 180	Arg	Gly	Ile	Gly	Asn 185	Gly	Ile	Ser	Ile 190	Ile	Ile	Phe
Ala	Gly	Ile 195	Val	Ala	Gly	Leu	Pro 200	Pro	Ala	Ile	Ala	His 205	Thr	Ile	Glu
Gln	Ala 210	Arg	Gln	Gly	Asp	Leu 215	His	Phe	Leu	Val	Leu 220	Leu	Leu	Val	Ala
Val 225	Leu	Val	Phe	Ala 230	Val	Thr	Phe	Phe	Val 235	Val	Phe	Val	Glu	Arg	Gly

Gln Arg Arg Ile Val Val Asn Tyr Ala Lys Arg Gln Gln Gly Arg Arg
 245 250 255
 Val Tyr Ala Ala Gln Ser Thr His Leu Pro Leu Lys Val Asn Met Ala
 260 265 270
 Gly Val Ile Pro Ala Ile Phe Ala Ser Ser Ile Ile Leu Phe Pro Ala
 275 280 285
 Thr Ile Ala Ser Trp Phe Gly Gly Gly Thr Gly Trp Asn Trp Leu Thr
 290 295 300
 Thr Ile Ser Leu Tyr Leu Gln Pro Gly Gln Pro Leu Tyr Val Leu Leu
 305 310 315 320
 Tyr Ala Ser Ala Ile Ile Phe Phe Cys Phe Phe Tyr Thr Ala Leu Val
 325 330 335
 Phe Asn Pro Arg Glu Thr Ala Asp Asn Leu Lys Lys Ser Gly Ala Phe
 340 345 350
 Val Pro Gly Ile Arg Pro Gly Glu Gln Thr Ala Lys Tyr Ile Asp Lys
 355 360 365
 Val Met Thr Arg Leu Thr Leu Val Gly Ala Leu Tyr Ile Thr Phe Ile
 370 375 380
 Cys Leu Ile Pro Glu Phe Met Arg Asp Ala Met Lys Val Pro Phe Tyr
 385 390 395 400
 Phe Gly Gly Thr Ser Leu Leu Ile Val Val Val Val Ile Met Asp Phe
 405 410 415
 Met Ala Gln Val Gln Thr Leu Met Met Ser Ser Gln Tyr Glu Ser Ala
 420 425 430
 Leu Lys Lys Ala Asn Leu Lys Gly Tyr Gly Arg
 435 440

<210> 313
 <211> 144
 <212> PRT
 <213> E. Coli

<400> 313
 Met Arg Leu Asn Thr Leu Ser Pro Ala Glu Gly Ser Lys Lys Ala Gly
 1 5 10 15
 Lys Arg Leu Gly Arg Gly Ile Gly Ser Gly Leu Gly Lys Thr Gly Gly
 20 25 30
 Arg Gly His Lys Gly Gln Lys Ser Arg Ser Gly Gly Gly Val Arg Arg
 35 40 45
 Gly Phe Glu Gly Gly Gln Met Pro Leu Tyr Arg Arg Leu Pro Lys Phe
 50 55 60
 Gly Phe Thr Ser Arg Lys Ala Ala Ile Thr Ala Glu Ile Arg Leu Ser
 65 70 75 80
 Asp Leu Ala Lys Val Glu Gly Gly Val Val Asp Leu Asn Thr Leu Lys
 85 90 95
 Ala Ala Asn Ile Ile Gly Ile Gln Ile Glu Phe Ala Lys Val Ile Leu
 100 105 110
 Ala Gly Glu Val Thr Thr Pro Val Thr Val Arg Gly Leu Arg Val Thr
 115 120 125
 Lys Gly Ala Arg Ala Ala Ile Glu Ala Ala Gly Gly Lys Ile Glu Glu
 130 135 140

<210> 314
 <211> 59

<212> PRT
<213> E. Coli

<400> 314

```

Met Ala Lys Thr Ile Lys Ile Thr Gln Thr Arg Ser Ala Ile Gly Arg
 1           5           10           15
Leu Pro Lys His Lys Ala Thr Leu Leu Gly Leu Gly Leu Arg Arg Ile
          20           25           30
Gly His Thr Val Glu Arg Glu Asp Thr Pro Ala Ile Arg Gly Met Ile
          35           40           45
Asn Ala Val Ser Phe Met Val Lys Val Glu Glu
 50           55

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<210> 315
<211> 167
<212> PRT
<213> E. Coli

<400> 315

```

Met Ala His Ile Glu Lys Gln Ala Gly Glu Leu Gln Glu Lys Leu Ile
 1           5           10           15
Ala Val Asn Arg Val Ser Lys Thr Val Lys Gly Gly Arg Ile Phe Ser
          20           25           30
Phe Thr Ala Leu Thr Val Val Gly Asp Gly Asn Gly Arg Val Gly Phe
          35           40           45
Gly Tyr Gly Lys Ala Arg Glu Val Pro Ala Ala Ile Gln Lys Ala Met
          50           55           60
Glu Lys Ala Arg Arg Asn Met Ile Asn Val Ala Leu Asn Asn Gly Thr
          65           70           75           80
Leu Gln His Pro Val Lys Gly Val His Thr Gly Ser Arg Val Phe Met
          85           90           95
Gln Pro Ala Ser Glu Gly Thr Gly Ile Ile Ala Gly Gly Ala Met Arg
          100          105          110
Ala Val Leu Glu Val Ala Gly Val His Asn Val Leu Ala Lys Ala Tyr
          115          120          125
Gly Ser Thr Asn Pro Ile Asn Val Val Arg Ala Thr Ile Asp Gly Leu
          130          135          140
Glu Asn Met Asn Ser Pro Glu Met Val Ala Ala Lys Arg Gly Lys Ser
          145          150          155          160
Val Glu Glu Ile Leu Gly Lys
          165

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<210> 316
<211> 117
<212> PRT
<213> E. Coli

<400> 316

```

Met Asp Lys Lys Ser Ala Arg Ile Arg Arg Ala Thr Arg Ala Arg Arg
 1           5           10           15
Lys Leu Gln Glu Leu Gly Ala Thr Arg Leu Val Val His Arg Thr Pro
          20           25           30
Arg His Ile Tyr Ala Gln Val Ile Ala Pro Asn Gly Ser Glu Val Leu
          35           40           45

```


Val Ala Ala Ser Thr Val Glu Lys Ala Ile Ala Glu Gln Leu Lys Tyr
 50 55 60
 Thr Gly Asn Lys Asp Ala Ala Ala Val Gly Lys Ala Val Ala Glu
 65 70 75 80
 Arg Ala Leu Glu Lys Gly Ile Lys Asp Val Ser Phe Asp Arg Ser Gly
 85 90 95
 Phe Gln Tyr His Gly Arg Val Gln Ala Leu Ala Asp Ala Ala Arg Glu
 100 105 110
 Ala Gly Leu Gln Phe
 115

<210> 317

<211> 177

<212> PRT

<213> E. Coli

<400> 317

Met Ser Arg Val Ala Lys Ala Pro Val Val Val Pro Ala Gly Val Asp
 1 5 10 15
 Val Lys Ile Asn Gly Gln Val Ile Thr Ile Lys Gly Lys Asn Gly Glu
 20 25 30
 Leu Thr Arg Thr Leu Asn Asp Ala Val Glu Val Lys His Ala Asp Asn
 35 40 45
 Thr Leu Thr Phe Gly Pro Arg Asp Gly Tyr Ala Asp Gly Trp Ala Gln
 50 55 60
 Ala Gly Thr Ala Arg Ala Leu Leu Asn Ser Met Val Ile Gly Val Thr
 65 70 75 80
 Glu Gly Phe Thr Lys Lys Leu Gln Leu Val Gly Val Gly Tyr Arg Ala
 85 90 95
 Ala Val Lys Gly Asn Val Ile Asn Leu Ser Leu Gly Phe Ser His Pro
 100 105 110
 Val Asp His Gln Leu Pro Ala Gly Ile Thr Ala Glu Cys Pro Thr Gln
 115 120 125
 Thr Glu Ile Val Leu Lys Gly Ala Asp Lys Gln Val Ile Gly Gln Val
 130 135 140
 Ala Ala Asp Leu Arg Ala Tyr Arg Arg Pro Glu Pro Tyr Lys Gly Lys
 145 150 155 160
 Gly Val Arg Tyr Ala Asp Glu Val Val Arg Thr Lys Glu Ala Lys Lys
 165 170 175
 Lys

<210> 318

<211> 130

<212> PRT

<213> E. Coli

<400> 318

Met Ser Met Gln Asp Pro Ile Ala Asp Met Leu Thr Arg Ile Arg Asn
 1 5 10 15
 Gly Gln Ala Ala Asn Lys Ala Ala Val Thr Met Pro Ser Ser Lys Leu
 20 25 30
 Lys Val Ala Ile Ala Asn Val Leu Lys Glu Glu Gly Phe Ile Glu Asp
 35 40 45
 Phe Lys Val Glu Gly Asp Thr Lys Pro Glu Leu Glu Leu Thr Leu Lys

50 55 60
 Tyr Phe Gln Gly Lys Ala Val Val Glu Ser Ile Gln Arg Val Ser Arg
 65 70 75 80
 Pro Gly Leu Arg Ile Tyr Lys Arg Lys Asp Glu Leu Pro Lys Val Met
 85 90 95
 Ala Gly Leu Gly Ile Ala Val Val Ser Thr Ser Lys Gly Val Met Thr
 100 105 110
 Asp Arg Ala Ala Arg Gln Ala Gly Leu Gly Gly Glu Ile Ile Cys Tyr
 115 120 125
 Val Ala
 130

<210> 319
 <211> 101
 <212> PRT
 <213> E. Coli

<400> 319
 Met Ala Lys Gln Ser Met Lys Ala Arg Glu Val Lys Arg Val Ala Leu
 1 5 10 15
 Ala Asp Lys Tyr Phe Ala Lys Arg Ala Glu Leu Lys Ala Ile Ile Ser
 20 25 30
 Asp Val Asn Ala Ser Asp Glu Asp Arg Trp Asn Ala Val Leu Lys Leu
 35 40 45
 Gln Thr Leu Pro Arg Asp Ser Ser Pro Ser Arg Gln Arg Asn Arg Cys
 50 55 60
 Arg Gln Thr Gly Arg Pro His Gly Phe Leu Arg Lys Phe Gly Leu Ser
 65 70 75 80
 Arg Ile Lys Val Arg Glu Ala Ala Met Arg Gly Glu Ile Pro Gly Leu
 85 90 95
 Lys Lys Ala Ser Trp
 100

<210> 320
 <211> 179
 <212> PRT
 <213> E. Coli

<400> 320
 Met Ala Lys Leu His Asp Tyr Tyr Lys Asp Glu Val Val Lys Lys Leu
 1 5 10 15
 Met Thr Glu Phe Asn Tyr Asn Ser Val Met Gln Val Pro Arg Val Glu
 20 25 30
 Lys Ile Thr Leu Asn Met Gly Val Gly Glu Ala Ile Ala Asp Lys Lys
 35 40 45
 Leu Leu Asp Asn Ala Ala Ala Asp Leu Ala Ala Ile Ser Gly Gln Lys
 50 55 60
 Pro Leu Ile Thr Lys Ala Arg Lys Ser Val Ala Gly Phe Lys Ile Arg
 65 70 75 80
 Gln Gly Tyr Pro Ile Gly Cys Lys Val Thr Leu Arg Gly Glu Arg Met
 85 90 95
 Trp Glu Phe Phe Glu Arg Leu Ile Thr Ile Ala Val Pro Arg Ile Arg
 100 105 110
 Asp Phe Arg Gly Leu Ser Ala Lys Ser Phe Asp Gly Arg Gly Asn Tyr

```

      115              120              125
Ser Met Gly Val Arg Glu Gln Ile Ile Phe Pro Glu Ile Asp Tyr Asp
      130              135              140
Lys Val Asp Arg Val Arg Gly Leu Asp Ile Thr Ile Thr Thr Thr Ala
      145              150              155              160
Lys Ser Asp Glu Glu Gly Arg Ala Leu Leu Ala Ala Phe Asp Phe Pro
      165              170              175
Phe Arg Lys

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<210> 321Z
<211> 104
<212> PRT
<213> E. Coli

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```

      <400> 321
Met Ala Ala Lys Ile Arg Arg Asp Asp Glu Val Ile Val Leu Thr Gly
      1              5              10              15
Lys Asp Lys Gly Lys Arg Gly Lys Val Lys Asn Val Leu Ser Ser Gly
      20              25              30
Lys Val Ile Val Glu Gly Ile Asn Leu Val Lys Lys His Gln Lys Pro
      35              40              45
Val Pro Ala Leu Asn Gln Pro Gly Gly Ile Val Glu Lys Glu Ala Ala
      50              55              60
Ile Gln Val Ser Asn Val Ala Ile Phe Asn Ala Ala Thr Gly Lys Ala
      65              70              75              80
Asp Arg Val Gly Phe Arg Phe Glu Asp Gly Lys Lys Val Arg Phe Phe
      85              90              95
Lys Ser Asn Ser Glu Thr Ile Lys
      100

```

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<210> 322
<211> 123
<212> PRT
<213> E. Coli

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      <400> 322
Met Ile Gln Glu Gln Thr Met Leu Asn Val Ala Asp Asn Ser Gly Ala
      1              5              10              15
Arg Arg Val Met Cys Ile Lys Val Leu Gly Gly Ser His Arg Arg Tyr
      20              25              30
Ala Gly Val Gly Asp Ile Ile Lys Ile Thr Ile Lys Glu Ala Ile Pro
      35              40              45
Arg Gly Lys Val Lys Lys Gly Asp Val Leu Lys Ala Val Val Val Arg
      50              55              60
Thr Lys Lys Gly Val Arg Arg Pro Asp Gly Ser Val Ile Arg Phe Asp
      65              70              75              80
Gly Asn Ala Cys Val Leu Leu Asn Asn Asn Ser Glu Gln Pro Ile Gly
      85              90              95
Thr Arg Ile Phe Gly Pro Val Thr Arg Glu Leu Arg Ser Glu Lys Phe
      100              105              110
Met Lys Ile Ile Ser Leu Ala Pro Glu Val Leu
      115              120

```

<210> 323
 <211> 188
 <212> PRT
 <213> E. Coli

<400> 323

Met	Phe	Lys	Gly	Gln	Lys	Thr	Leu	Ala	Ala	Leu	Ala	Val	Ser	Leu	Leu
1				5					10					15	
Phe	Thr	Ala	Pro	Val	Tyr	Ala	Ala	Asp	Glu	Gly	Ser	Gly	Glu	Ile	His
			20					25					30		
Phe	Lys	Gly	Glu	Val	Ile	Glu	Ala	Pro	Cys	Glu	Ile	His	Pro	Glu	Asp
		35					40					45			
Ile	Asp	Lys	Asn	Ile	Asp	Leu	Gly	Gln	Val	Thr	Thr	Thr	His	Ile	Asn
	50					55					60				
Arg	Glu	His	His	Ser	Asn	Lys	Val	Ala	Val	Asp	Ile	Arg	Leu	Ile	Asn
65					70					75					80
Cys	Asp	Leu	Pro	Ala	Ser	Asp	Asn	Gly	Ser	Gly	Met	Pro	Val	Ser	Lys
				85					90					95	
Val	Gly	Val	Thr	Phe	Asp	Ser	Thr	Ala	Lys	Thr	Thr	Gly	Ala	Thr	Pro
			100					105					110		
Leu	Leu	Ser	Asn	Thr	Ser	Ala	Gly	Glu	Ala	Thr	Gly	Val	Gly	Val	Arg
		115					120					125			
Leu	Met	Asp	Lys	Asn	Asp	Gly	Asn	Ile	Val	Leu	Gly	Ser	Ala	Ala	Pro
	130					135					140				
Asp	Leu	Asp	Leu	Asp	Ala	Ser	Ser	Ser	Glu	Gln	Thr	Leu	Asn	Phe	Phe
145					150					155					160
Ala	Trp	Met	Glu	Gln	Ile	Asp	Asn	Ala	Val	Asp	Val	Thr	Ala	Gly	Glu
				165					170					175	
Val	Thr	Ala	Asn	Ala	Thr	Tyr	Val	Leu	Asp	Tyr	Lys				
			180					185							

<210> 324
 <211> 427
 <212> PRT
 <213> E. Coli

<400> 324

Met	Ala	Asp	Thr	Lys	Ala	Lys	Leu	Thr	Leu	Asn	Gly	Asp	Thr	Ala	Val
1				5					10					15	
Glu	Leu	Asp	Val	Leu	Lys	Gly	Thr	Leu	Gly	Gln	Asp	Val	Ile	Asp	Ile
			20					25					30		
Arg	Thr	Leu	Gly	Ser	Lys	Gly	Val	Phe	Thr	Phe	Asp	Pro	Gly	Phe	Thr
		35					40					45			
Ser	Thr	Ala	Ser	Cys	Glu	Ser	Lys	Ile	Thr	Phe	Ile	Asp	Gly	Asp	Glu
	50					55					60				
Gly	Ile	Leu	Leu	His	Arg	Gly	Phe	Pro	Ile	Asp	Gln	Leu	Ala	Thr	Asp
65				70						75					80
Ser	Asn	Tyr	Leu	Glu	Val	Cys	Tyr	Ile	Leu	Leu	Asn	Gly	Glu	Lys	Pro
				85					90					95	
Thr	Gln	Glu	Gln	Tyr	Asp	Glu	Phe	Lys	Thr	Thr	Val	Thr	Arg	His	Thr
			100					105					110		
Met	Ile	His	Glu	Gln	Ile	Thr	Arg	Leu	Phe	His	Ala	Phe	Arg	Arg	Asp
		115					120					125			
Ser	His	Pro	Met	Ala	Val	Met	Cys	Gly	Ile	Thr	Gly	Ala	Leu	Ala	Ala
	130					135					140				
Phe	Tyr	His	Asp	Ser	Leu	Asp	Val	Asn	Asn	Pro	Arg	His	Arg	Glu	Ile

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145          150          155          160
Ala Ala Phe Arg Leu Leu Ser Lys Met Pro Thr Met Ala Ala Met Cys
165          170          175
Tyr Lys Tyr Ser Ile Gly Gln Pro Phe Val Tyr Pro Arg Asn Asp Leu
180          185          190
Ser Tyr Ala Gly Asn Phe Leu Asn Met Met Phe Ser Thr Pro Cys Glu
195          200          205
Pro Tyr Glu Val Asn Pro Ile Leu Glu Arg Ala Met Asp Arg Ile Leu
210          215          220
Ile Leu His Ala Asp His Glu Gln Asn Ala Ser Thr Ser Thr Val Arg
225          230          235
Thr Ala Gly Ser Ser Gly Ala Asn Pro Phe Ala Cys Ile Ala Ala Gly
245          250          255
Ile Ala Ser Leu Trp Gly Pro Ala His Gly Gly Ala Asn Glu Ala Ala
260          265          270
Leu Lys Met Leu Glu Glu Ile Ser Ser Val Lys His Ile Pro Glu Phe
275          280          285
Val Arg Arg Ala Lys Asp Lys Asn Asp Ser Phe Arg Leu Met Gly Phe
290          295          300
Gly His Arg Val Tyr Lys Asn Tyr Asp Pro Arg Ala Thr Val Met Arg
305          310          315
Glu Thr Cys His Glu Val Leu Lys Glu Leu Gly Thr Lys Asp Asp Leu
325          330          335
Leu Glu Val Ala Met Glu Leu Glu Asn Ile Ala Leu Asn Asp Pro Tyr
340          345          350
Phe Ile Glu Lys Lys Leu Tyr Pro Asn Val Asp Phe Tyr Ser Gly Ile
355          360          365
Ile Leu Lys Ala Met Gly Ile Pro Ser Ser Met Phe Thr Val Ile Phe
370          375          380
Ala Met Ala Arg Thr Val Gly Trp Ile Ala His Trp Ser Glu Met His
385          390          395
Ser Asp Gly Met Lys Ile Ala Arg Pro Arg Gln Leu Tyr Thr Gly Tyr
405          410          415
Glu Lys Arg Asp Phe Lys Ser Asp Ile Lys Arg
420          425

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<210> 325
<211> 477
<212> PRT
<213> E. Coli

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```

<400> 325
Met Lys Val Thr Leu Pro Glu Phe Glu Arg Ala Gly Val Met Val Val
1      5      10
Gly Asp Val Met Leu Asp Arg Tyr Trp Tyr Gly Pro Thr Ser Arg Ile
20     25     30
Ser Pro Glu Ala Pro Val Pro Val Lys Val Asn Thr Ile Glu Glu
35     40     45
Arg Pro Gly Gly Ala Ala Asn Val Ala Met Asn Ile Ala Ser Leu Gly
50     55     60
Ala Asn Ala Arg Leu Val Gly Leu Thr Gly Ile Asp Asp Ala Ala Arg
65     70     75     80
Ala Leu Ser Lys Ser Leu Ala Asp Val Asn Val Lys Cys Asp Phe Val
85     90     95
Ser Val Pro Thr His Pro Thr Ile Thr Lys Leu Arg Val Leu Ser Arg
100    105    110

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002210-60226460

```

Asn Gln Gln Leu Ile Arg Leu Asp Phe Glu Glu Gly Phe Glu Gly Val
    115                120                125
Asp Pro Gln Pro Leu His Glu Arg Ile Asn Gln Ala Leu Ser Ser Ile
    130                135                140
Gly Ala Leu Val Leu Ser Asp Tyr Ala Lys Gly Ala Leu Ala Ser Val
    145                150                155                160
Gln Gln Met Ile Gln Leu Ala Arg Lys Ala Gly Val Pro Val Leu Ile
    165                170                175
Asp Pro Lys Gly Thr Asp Phe Glu Arg Tyr Arg Gly Ala Thr Leu Leu
    180                185                190
Thr Pro Asn Leu Ser Glu Phe Glu Ala Val Val Gly Lys Cys Lys Thr
    195                200                205
Glu Glu Glu Ile Val Glu Arg Gly Met Lys Leu Ile Ala Asp Tyr Glu
    210                215                220
Leu Ser Ala Leu Leu Val Thr Arg Ser Glu Gln Gly Met Ser Leu Leu
    225                230                235                240
Gln Pro Gly Lys Ala Pro Leu His Met Pro Thr Gln Ala Gln Glu Val
    245                250                255
Tyr Asp Val Thr Gly Ala Gly Asp Thr Val Ile Gly Val Leu Ala Ala
    260                265                270
Thr Leu Ala Ala Gly Asn Ser Leu Glu Glu Ala Cys Phe Phe Ala Asn
    275                280                285
Ala Ala Ala Gly Val Val Val Gly Lys Leu Gly Thr Ser Thr Val Ser
    290                295                300
Pro Ile Glu Leu Glu Asn Ala Val Arg Gly Arg Ala Asp Thr Gly Phe
    305                310                315                320
Gly Val Met Thr Glu Glu Glu Leu Lys Leu Ala Val Ala Ala Ala Arg
    325                330                335
Lys Arg Gly Glu Lys Val Val Met Thr Asn Gly Val Phe Asp Ile Leu
    340                345                350
His Ala Gly His Val Ser Tyr Leu Ala Asn Ala Arg Lys Leu Gly Asp
    355                360                365
Arg Leu Ile Val Ala Val Asn Ser Asp Ala Ser Thr Lys Arg Leu Lys
    370                375                380
Gly Asp Ser Arg Pro Val Asn Pro Leu Glu Gln Arg Met Ile Val Leu
    385                390                395                400
Gly Ala Leu Glu Ala Val Asp Trp Val Val Ser Phe Glu Glu Asp Thr
    405                410                415
Pro Gln Arg Leu Ile Ala Gly Ile Leu Pro Asp Leu Leu Val Lys Gly
    420                425                430
Gly Asp Tyr Lys Pro Glu Glu Ile Ala Gly Ser Lys Glu Val Trp Ala
    435                440                445
Asn Gly Gly Glu Val Leu Val Leu Asn Phe Glu Asp Gly Cys Ser Thr
    450                455                460
Thr Asn Ile Ile Lys Lys Ile Gln Gln Asp Lys Lys Gly
    465                470                475

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<210> 326
 <211> 946
 <212> PRT
 <213> E. Coli

<400> 326
 Met Lys Pro Leu Ser Ser Pro Leu Gln Gln Tyr Trp Gln Thr Val Val
 1 5 10 15
 Glu Arg Leu Pro Glu Pro Leu Ala Glu Glu Ser Leu Ser Ala Gln Ala

Lys	Ser	Val	Leu	Thr	Phe	Ser	Asp	Phe	Val	Gln	Asp	Ser	Val	Ile	Ala
		35					40					45			
His	Pro	Glu	Trp	Leu	Thr	Glu	Leu	Glu	Ser	Gln	Pro	Pro	Gln	Ala	Asp
	50					55					60				
Glu	Trp	Gln	His	Tyr	Ala	Ala	Trp	Leu	Gln	Glu	Ala	Leu	Cys	Asn	Val
65					70					75					80
Ser	Asp	Glu	Ala	Gly	Leu	Met	Arg	Glu	Leu	Arg	Leu	Phe	Arg	Arg	Arg
				85					90					95	
Ile	Met	Val	Arg	Ile	Ala	Trp	Ala	Gln	Thr	Leu	Ala	Leu	Val	Thr	Gln
			100					105					110		
Glu	Ser	Ile	Leu	Gln	Gln	Leu	Ser	Tyr	Leu	Ala	Glu	Thr	Leu	Ile	Val
		115					120					125			
Ala	Ala	Arg	Asp	Trp	Leu	Tyr	Asp	Ala	Cys	Cys	Arg	Glu	Trp	Gly	Thr
	130					135					140				
Pro	Cys	Asn	Ala	Gln	Gly	Glu	Ala	Gln	Pro	Leu	Ile	Leu	Gly	Met	
145					150					155				160	
Gly	Lys	Leu	Gly	Gly	Gly	Glu	Leu	Asn	Phe	Ser	Ser	Asp	Ile	Asp	Leu
				165					170					175	
Ile	Phe	Ala	Trp	Pro	Glu	His	Gly	Cys	Thr	Gln	Gly	Gly	Arg	Arg	Glu
			180					185					190		
Leu	Asp	Asn	Ala	Gln	Phe	Phe	Thr	Arg	Met	Gly	Gln	Arg	Leu	Ile	Lys
		195					200					205			
Val	Leu	Asp	Gln	Pro	Thr	Gln	Asp	Gly	Phe	Val	Tyr	Arg	Val	Asp	Met
	210					215					220				
Arg	Leu	Arg	Pro	Phe	Gly	Glu	Ser	Gly	Pro	Leu	Val	Leu	Ser	Phe	Ala
225					230					235				240	
Ala	Leu	Glu	Asp	Tyr	Tyr	Gln	Glu	Gln	Gly	Arg	Asp	Trp	Glu	Arg	Tyr
				245					250					255	
Ala	Met	Val	Lys	Ala	Arg	Ile	Met	Gly	Asp	Ser	Glu	Gly	Val	Tyr	Ala
			260					265					270		
Asn	Glu	Leu	Arg	Ala	Met	Leu	Arg	Pro	Phe	Val	Phe	Arg	Arg	Tyr	Ile
		275					280					285			
Asp	Phe	Ser	Val	Ile	Gln	Ser	Leu	Arg	Asn	Met	Lys	Gly	Met	Ile	Ala
	290					295					300				
Arg	Glu	Val	Arg	Arg	Arg	Gly	Leu	Thr	Asp	Asn	Ile	Lys	Leu	Gly	Ala
305					310					315					320
Gly	Gly	Ile	Arg	Glu	Ile	Glu	Phe	Ile	Val	Gln	Val	Phe	Gln	Leu	Ile
				325					330					335	
Arg	Gly	Gly	Arg	Glu	Pro	Ser	Leu	Gln	Ser	Arg	Ser	Leu	Leu	Pro	Thr
			340					345					350		
Leu	Ser	Ala	Ile	Ala	Glu	Leu	His	Leu	Leu	Ser	Glu	Asn	Asp	Ala	Glu
		355					360					365			
Gln	Leu	Arg	Val	Ala	Tyr	Leu	Phe	Leu	Arg	Arg	Leu	Glu	Asn	Leu	Leu
	370					375									

Leu Thr Leu Ile Ala Asp Phe Arg Lys Glu Leu Asp Lys Arg Thr Ile
 485 490 495
 Gly Pro Arg Gly Arg Gln Val Leu Asp His Leu Met Pro His Leu Leu
 500 505 510
 Ser Asp Val Cys Ala Arg Glu Asp Ala Ala Val Thr Leu Ser Arg Ile
 515 520 525
 Thr Ala Leu Leu Val Gly Ile Val Thr Arg Thr Thr Tyr Leu Glu Leu
 530 535 540
 Leu Ser Glu Phe Pro Ala Ala Leu Lys His Leu Ile Ser Leu Cys Ala
 545 550 555 560
 Ala Ser Pro Met Ile Ala Ser Gln Leu Ala Arg Tyr Pro Leu Leu Leu
 565 570 575
 Asp Glu Leu Leu Asp Pro Asn Thr Leu Tyr Gln Pro Thr Ala Thr Asp
 580 585 590
 Ala Tyr Arg Asp Glu Leu Arg Gln Tyr Leu Leu Arg Val Pro Glu Asp
 595 600 605
 Asp Glu Glu Gln Gln Leu Glu Ala Leu Arg Gln Phe Lys Gln Ala Gln
 610 615 620
 Leu Leu Arg Ile Ala Ala Ala Asp Ile Ala Gly Thr Leu Pro Val Met
 625 630 635 640
 Lys Val Ser Asp His Leu Thr Trp Leu Ala Glu Ala Met Ile Asp Ala
 645 650 655
 Val Val Gln Gln Ala Trp Val Gln Met Val Ala Arg Tyr Gly Lys Pro
 660 665 670
 Asn His Leu Asn Glu Arg Glu Gly Arg Gly Phe Ala Val Val Gly Tyr
 675 680 685
 Gly Lys Leu Gly Gly Trp Glu Leu Gly Tyr Ser Ser Asp Leu Asp Leu
 690 695 700
 Ile Phe Leu His Asp Cys Pro Met Asp Ala Met Thr Asp Gly Glu Arg
 705 710 715 720
 Glu Ile Asp Gly Arg Gln Phe Tyr Leu Arg Leu Ala Gln Arg Ile Met
 725 730 735
 His Leu Phe Ser Thr Arg Thr Ser Ser Gly Ile Leu Tyr Glu Val Asp
 740 745 750
 Ala Arg Leu Arg Pro Ser Gly Ala Ala Gly Met Leu Val Thr Ser Ala
 755 760 765
 Glu Ala Phe Ala Asp Tyr Gln Lys Asn Glu Ala Trp Thr Trp Glu His
 770 775 780
 Gln Ala Leu Val Arg Ala Arg Val Val Tyr Gly Asp Pro Gln Leu Thr
 785 790 795 800
 Ala His Phe Asp Ala Val Arg Arg Glu Ile Met Thr Leu Pro Arg Glu
 805 810 815
 Gly Lys Thr Leu Gln Thr Glu Val Arg Glu Met Arg Glu Lys Met Arg
 820 825 830
 Ala His Leu Gly Asn Lys His Arg Asp Arg Phe Asp Ile Lys Ala Asp
 835 840 845
 Glu Gly Gly Ile Thr Asp Ile Glu Phe Ile Thr Gln Tyr Leu Val Leu
 850 855 860
 Arg Tyr Ala His Glu Lys Pro Lys Leu Thr Arg Trp Ser Asp Asn Val
 865 870 875 880
 Arg Ile Leu Glu Leu Leu Ala Gln Asn Asp Ile Met Glu Glu Gln Glu
 885 890 895
 Ala Met Ala Leu Thr Arg Ala Tyr Thr Thr Leu Arg Asp Glu Leu His
 900 905 910
 His Leu Ala Leu Gln Glu Leu Pro Gly His Val Ser Glu Asp Cys Phe
 915 920 925
 Thr Ala Glu Arg Glu Leu Val Arg Ala Ser Trp Gln Lys Trp Leu Val

930
Glu Glu
945

935

940

<210> 327
<211> 433
<212> PRT
<213> E. Coli

<400> 327

Met Ala Gln Glu Ile Glu Leu Lys Phe Ile Val Asn His Ser Ala Val
1 5 10 15
Glu Ala Leu Arg Asp His Leu Asn Thr Leu Gly Gly Glu His His Asp
20 25 30
Pro Val Gln Leu Leu Asn Ile Tyr Tyr Glu Thr Pro Asp Asn Trp Leu
35 40 45
Arg Gly His Asp Met Gly Leu Arg Ile Arg Gly Glu Asn Gly Arg Tyr
50 55 60
Glu Met Thr Met Lys Val Ala Gly Arg Val Thr Gly Gly Leu His Gln
65 70 75 80
Arg Pro Glu Tyr Asn Val Ala Leu Ser Glu Pro Thr Leu Asp Leu Ala
85 90 95
Gln Leu Pro Thr Glu Val Trp Pro Asn Gly Glu Leu Pro Ala Asp Leu
100 105 110
Ala Ser Arg Val Gln Pro Leu Phe Ser Thr Asp Phe Tyr Arg Glu Lys
115 120 125
Trp Leu Val Ala Val Asp Gly Ser Gln Ile Glu Ile Ala Leu Asp Gln
130 135 140
Gly Glu Val Lys Ala Gly Glu Phe Ala Glu Pro Ile Cys Glu Leu Glu
145 150 155 160
Leu Glu Leu Leu Ser Gly Asp Thr Arg Ala Val Leu Lys Leu Ala Asn
165 170 175
Gln Leu Val Ser Gln Thr Gly Leu Arg Gln Gly Ser Leu Ser Lys Ala
180 185 190
Ala Arg Gly Tyr His Leu Ala Gln Gly Asn Pro Ala Arg Glu Ile Lys
195 200 205
Pro Thr Thr Ile Leu His Val Ala Ala Lys Ala Asp Val Glu Gln Gly
210 215 220
Leu Glu Ala Ala Leu Glu Leu Ala Leu Ala Gln Trp Gln Tyr His Glu
225 230 235 240
Glu Leu Trp Val Arg Gly Asn Asp Ala Ala Lys Glu Gln Val Leu Ala
245 250 255
Ala Ile Ser Leu Val Arg His Thr Leu Met Leu Phe Gly Gly Ile Val
260 265 270
Pro Arg Lys Ala Ser Thr His Leu Arg Asp Leu Leu Thr Gln Cys Glu
275 280 285
Ala Thr Ile Ala Ser Ala Val Ser Ala Val Thr Ala Val Tyr Ser Thr
290 295 300
Glu Thr Ala Met Ala Lys Leu Ala Leu Thr Glu Trp Leu Val Ser Lys
305 310 315 320
Ala Trp Gln Pro Phe Leu Asp Ala Lys Ala Gln Gly Lys Ile Ser Asp
325 330 335
Ser Phe Lys Arg Phe Ala Asp Ile His Leu Ser Arg His Ala Ala Glu
340 345 350
Leu Lys Ser Val Phe Cys Gln Pro Leu Gly Asp Arg Tyr Arg Asp Gln

002270 60226460


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Leu Leu Val Ile Asn Pro Gly Asn Asn Asn Asp Lys Gln Phe Ser Leu
145          150          155          160
Leu Leu Glu Glu Tyr Arg Ser Leu Phe Gly Leu Ala Ser Leu Arg Phe
          165          170          175
Gln Gly Asp Gln His Leu Leu Asp Ile Ala Phe Trp Cys Asn Glu Lys
          180          185          190
Gly Val Ser Ala Arg Gln Gln Leu Ser Val Gln Gln Gln Asn Gly Ile
          195          200          205
Trp Thr Leu Val Gln Ser Glu Glu Ala Glu Ile Gln Pro Arg Ser Asp
          210          215          220
Glu Lys Arg Ile Leu Ser Asn Val Ala Val Leu Glu Gly Ala Pro Pro
          225          230          235          240
Leu Ser Glu His Trp Gln Leu Phe Asn Asn Asn Glu Val Leu Phe Asn
          245          250          255
Glu Ala Arg Thr Ala Gln Ala Ala Thr Val Val Phe Ser Leu Gln Gln
          260          265          270
Asn Ala Gln Ile Glu Pro Leu Ala Arg Ser Ile His Thr Leu Arg Arg
          275          280          285
Gln Arg Gly Ser Ala Met Lys Ile Leu Val Arg Glu Asn Thr Ala Ser
          290          295          300
Leu Arg Ala Thr Asp Glu Arg Leu Leu Leu Ala Cys Gly Ala Asn Met
          305          310          315          320
Val Ile Pro Trp Asn Ala Pro Leu Ser Arg Cys Leu Thr Met Ile Glu
          325          330          335
Ser Val Gln Gly Gln Lys Phe Ser Arg Tyr Val Pro Glu Asp Ile Thr
          340          345          350
Thr Leu Leu Ser Met Thr Gln Pro Leu Lys Leu Arg Gly Phe Gln Lys
          355          360          365
Trp Asp Val Phe Cys Asn Ala Val Asn Asn Met Met Asn Asn Pro Leu
          370          375          380
Leu Pro Ala His Gly Lys Gly Val Leu Val Ala Leu Arg Pro Val Pro
          385          390          395          400
Gly Ile Arg Val Glu Gln Ala Leu Thr Leu Cys Arg Pro Asn Arg Thr
          405          410          415
Gly Asp Ile Met Thr Ile Gly Gly Asn Arg Leu Val Leu Phe Leu Ser
          420          425          430
Phe Cys Arg Ile Asn Asp Leu Asp Thr Ala Leu Asn His Ile Phe Pro
          435          440          445
Leu Pro Thr Gly Asp Ile Phe Ser Asn Arg Met Val Trp Phe Glu Asp
          450          455          460
Asp Gln Ile Ser Ala Glu Leu Val Gln Met Arg Leu Leu Ala Pro Glu
          465          470          475          480
Gln Trp Gly Met Pro Leu Pro Leu Thr Gln Ser Ser Lys Pro Val Ile
          485          490          495
Asn Ala Glu His Asp Gly Arg His Trp Arg Arg Ile Pro Glu Pro Met
          500          505          510
Arg Leu Leu Asp Asp Ala Val Glu Arg Ser Ser
          515          520

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<210> 330

<211> 62

<212> PRT

<213> E. Coli

<400> 330

Met Thr Ile Ser Asp Ile Ile Glu Ile Ile Val Val Cys Ala Leu Ile

1		5		10		15
Phe	Phe	Pro	Leu	Gly	Tyr	Leu
			20			25
Asp	Thr	Leu	Arg	Leu	Phe	Phe
		35			40	
Gly	Thr	Leu	Arg	Arg	Thr	Glu
		50			55	
						60

<210> 331
 <211> 559
 <212> PRT
 <213> E. Coli

<400> 331

Met	Thr	Gln	Phe	Thr	Gln	Asn	Thr	Ala	Met	Pro	Ser	Ser	Leu	Trp	Gln
1				5					10					15	
Tyr	Trp	Arg	Gly	Leu	Ser	Gly	Trp	Asn	Phe	Tyr	Phe	Leu	Val	Lys	Phe
			20					25					30		
Gly	Leu	Leu	Trp	Ala	Gly	Tyr	Leu	Asn	Phe	His	Pro	Leu	Leu	Asn	Leu
		35				40						45			
Val	Phe	Ala	Ala	Phe	Leu	Leu	Met	Pro	Leu	Pro	Arg	Tyr	Ser	Leu	His
	50					55					60				
Arg	Leu	Arg	His	Trp	Ile	Ala	Leu	Pro	Ile	Gly	Phe	Ala	Leu	Phe	Trp
65				70						75					80
His	Asp	Thr	Trp	Leu	Pro	Gly	Pro	Glu	Ser	Ile	Met	Ser	Gln	Gly	Ser
			85						90					95	
Gln	Val	Ala	Gly	Phe	Ser	Thr	Asp	Tyr	Leu	Ile	Asp	Leu	Val	Thr	Arg
		100						105					110		
Phe	Ile	Asn	Trp	Gln	Met	Ile	Gly	Ala	Ile	Phe	Val	Leu	Leu	Val	Ala
		115					120					125			
Trp	Leu	Phe	Leu	Ser	Gln	Trp	Ile	Arg	Ile	Thr	Val	Phe	Val	Val	Ala
	130					135					140				
Ile	Leu	Leu	Trp	Leu	Asn	Val	Leu	Thr	Leu	Ala	Gly	Pro	Ser	Phe	Ser
145				150						155					160
Leu	Trp	Pro	Ala	Gly	Gln	Pro	Thr	Thr	Thr	Val	Thr	Thr	Thr	Gly	Gly
			165					170						175	
Asn	Ala	Ala	Ala	Thr	Val	Ala	Ala	Thr	Gly	Gly	Ala	Pro	Val	Val	Gly
		180						185					190		
Asp	Met	Pro	Ala	Gln	Thr	Ala	Pro	Pro	Thr	Thr	Ala	Asn	Leu	Asn	Ala
	195						200					205			
Trp	Leu	Asn	Asn	Phe	Tyr	Asn	Ala	Glu	Ala	Lys	Arg	Lys	Ser	Thr	Phe
	210					215					220				
Pro	Ser	Ser	Leu	Pro	Ala	Asp	Ala	Gln	Pro	Phe	Glu	Leu	Leu	Val	Ile
225				230						235					240
Asn	Ile	Cys	Ser	Leu	Ser	Trp	Ser	Asp	Ile	Glu	Ala	Ala	Gly	Leu	Met
			245						250					255	
Ser	His	Pro	Leu	Trp	Ser	His	Phe	Asp	Ile	Glu	Phe	Lys	Asn	Phe	Asn
		260						265					270		
Ser	Ala	Thr	Ser	Tyr	Ser	Gly	Pro	Ala	Ala	Ile	Arg	Leu	Leu	Arg	Ala
	275						280					285			
Ser	Cys	Gly	Gln	Thr	Ser	His	Thr	Asn	Leu	Tyr	Gln	Pro	Ala	Asn	Asn
	290					295					300				
Asp	Cys	Tyr	Leu	Phe	Asp	Asn	Leu	Ser	Lys	Leu	Gly	Phe	Thr	Gln	His
305				310						315					320
Leu	Met	Met	Gly	His	Asn	Gly	Gln	Phe	Gly	Gly	Phe	Leu	Lys	Glu	Val
				325					330					335	

Arg Glu Asn Gly Gly Met Gln Ser Glu Leu Met Asp Gln Thr Asn Leu
 340 345 350
 Pro Val Ile Leu Leu Gly Phe Asp Gly Ser Pro Val Tyr Asp Asp Thr
 355 360 365
 Ala Val Leu Asn Arg Trp Leu Asp Val Thr Glu Lys Asp Lys Asn Ser
 370 375 380
 Arg Ser Ala Thr Phe Tyr Asn Thr Leu Pro Leu His Asp Gly Asn His
 385 390 395 400
 Tyr Pro Gly Val Ser Lys Thr Ala Asp Tyr Lys Ala Arg Ala Gln Lys
 405 410 415
 Phe Phe Asp Glu Leu Asp Ala Phe Phe Thr Glu Leu Glu Lys Ser Gly
 420 425 430
 Arg Lys Val Met Val Val Val Val Pro Glu His Gly Gly Ala Leu Lys
 435 440 445
 Gly Asp Arg Met Gln Val Ser Gly Leu Arg Asp Ile Pro Ser Pro Ser
 450 455 460
 Ile Thr Asp Val Pro Val Gly Val Lys Phe Phe Gly Met Lys Ala Pro
 465 470 475 480
 His Gln Gly Ala Pro Ile Val Ile Glu Gln Pro Ser Ser Phe Leu Ala
 485 490 495
 Ile Ser Asp Leu Val Val Arg Val Leu Asp Gly Lys Ile Phe Thr Glu
 500 505 510
 Asp Asn Val Asp Trp Lys Lys Leu Thr Ser Gly Leu Pro Gln Thr Ala
 515 520 525
 Pro Val Ser Glu Asn Ser Asn Ala Val Val Ile Gln Tyr Gln Asp Lys
 530 535 540
 Pro Tyr Val Arg Leu Asn Gly Gly Asp Trp Val Pro Tyr Pro Gln
 545 550 555

<210> 332
 <211> 127
 <212> PRT
 <213> E. Coli

<400> 332
 Met Glu Gly Ser Arg Met Lys Tyr Arg Ile Ala Leu Ala Val Ser Leu
 1 5 10 15
 Phe Ala Leu Ser Ala Gly Ser Tyr Ala Thr Thr Leu Cys Gln Glu Lys
 20 25 30
 Glu Gln Asn Ile Leu Lys Glu Ile Ser Tyr Ala Glu Lys His Gln Asn
 35 40 45
 Gln Asn Arg Ile Asp Gly Leu Asn Lys Ala Leu Ser Glu Val Arg Ala
 50 55 60
 Asn Cys Ser Asp Ser Gln Leu Arg Ala Asp His Gln Lys Lys Ile Ala
 65 70 75 80
 Lys Gln Lys Asp Glu Val Ala Glu Arg Gln Gln Asp Leu Ala Glu Ala
 85 90 95
 Lys Gln Lys Gly Asp Ala Asp Lys Ile Ala Lys Arg Glu Arg Lys Leu
 100 105 110
 Ala Glu Ala Gln Glu Glu Leu Lys Lys Leu Glu Ala Arg Asp Tyr
 115 120 125

<210> 333
 <211> 101
 <212> PRT

<213> E. Coli

<400> 333

Met Ser Lys Glu His Thr Thr Glu His Leu Arg Ala Glu Leu Lys Ser
1 5 10 15
Leu Ser Asp Thr Leu Glu Glu Val Leu Ser Ser Ser Gly Glu Lys Ser
20 25 30
Lys Glu Glu Leu Ser Lys Ile Arg Ser Lys Ala Glu Gln Ala Leu Lys
35 40 45
Gln Ser Arg Tyr Arg Leu Gly Glu Thr Gly Asp Ala Ile Ala Lys Gln
50 55 60
Thr Arg Val Ala Ala Ala Arg Ala Asp Glu Tyr Val Arg Glu Asn Pro
65 70 75 80
Trp Thr Gly Val Gly Ile Gly Ala Ala Ile Gly Val Val Leu Gly Val
85 90 95
Leu Leu Ser Arg Arg
100

<210> 334

<211> 134

<212> PRT

<213> E. Coli

<400> 334

Met Ala Asp Thr His His Ala Gln Gly Pro Gly Lys Ser Val Leu Gly
1 5 10 15
Ile Gly Gln Arg Ile Val Ser Ile Met Val Glu Met Val Glu Thr Arg
20 25 30
Leu Arg Leu Ala Val Val Glu Leu Glu Glu Lys Ala Asn Leu Phe
35 40 45
Gln Leu Leu Leu Met Leu Gly Leu Thr Met Leu Phe Ala Ala Phe Gly
50 55 60
Leu Met Ser Leu Met Val Leu Ile Ile Trp Ala Val Asp Pro Gln Tyr
65 70 75 80
Arg Leu Asn Ala Met Ile Ala Thr Thr Val Val Leu Leu Leu Leu Ala
85 90 95
Leu Ile Gly Gly Ile Trp Thr Leu Arg Lys Ser Arg Lys Ser Thr Leu
100 105 110
Leu Arg His Thr Arg His Glu Leu Ala Asn Asp Arg Gln Leu Leu Glu
115 120 125
Glu Glu Ser Arg Glu Gln
130

<210> 335

<211> 99

<212> PRT

<213> E. Coli

<400> 335

Met Ser Ser Lys Val Glu Arg Glu Arg Arg Lys Ala Gln Leu Leu Ser
1 5 10 15
Gln Ile Gln Gln Gln Arg Leu Asp Leu Ser Ala Ser Arg Arg Glu Trp
20 25 30
Leu Glu Thr Thr Gly Ala Tyr Asp Arg Arg Trp Asn Met Leu Leu Ser

	35					40				45					
Leu	Arg	Ser	Trp	Ala	Leu	Val	Gly	Ser	Ser	Val	Met	Ala	Ile	Trp	Thr
50						55					60				
Ile	Arg	His	Pro	Asn	Met	Leu	Val	Arg	Trp	Ala	Arg	Arg	Gly	Phe	Gly
65					70					75				80	
Val	Trp	Ser	Ala	Trp	Arg	Leu	Val	Lys	Thr	Thr	Leu	Lys	Gln	Gln	Gln
				85					90					95	
Leu	Arg	Gly													

<210> 336
 <211> 160
 <212> PRT
 <213> E. Coli

Met	Ile	Leu	Ser	Ile	Asp	Ser	Asn	Asp	Ala	Asn	Thr	Ala	Pro	Leu	His
1				5					10					15	
Lys	Lys	Thr	Ile	Ser	Ser	Leu	Ser	Gly	Ala	Val	Glu	Ser	Met	Met	Lys
			20					25					30		
Lys	Leu	Glu	Asp	Val	Gly	Val	Leu	Val	Ala	Arg	Ile	Leu	Met	Pro	Ile
		35					40					45			
Leu	Phe	Ile	Thr	Ala	Gly	Trp	Gly	Lys	Ile	Thr	Gly	Tyr	Ala	Gly	Thr
50					55						60				
Gln	Gln	Tyr	Met	Glu	Ala	Met	Gly	Val	Pro	Gly	Phe	Met	Leu	Pro	Leu
65					70					75				80	
Val	Ile	Leu	Leu	Glu	Phe	Gly	Gly	Gly	Leu	Ala	Ile	Leu	Phe	Gly	Phe
				85					90					95	
Leu	Thr	Arg	Thr	Thr	Ala	Leu	Phe	Thr	Ala	Gly	Phe	Thr	Leu	Leu	Thr
			100					105					110		
Ala	Phe	Leu	Phe	His	Ser	Asn	Phe	Ala	Glu	Gly	Val	Asn	Ser	Leu	Met
		115					120					125			
Phe	Met	Lys	Asn	Leu	Thr	Ile	Ser	Gly	Gly	Phe	Leu	Leu	Leu	Ala	Ile
130						135					140				
Thr	Gly	Pro	Gly	Ala	Tyr	Ser	Ile	Asp	Arg	Leu	Leu	Asn	Lys	Lys	Trp
145					150					155					160

<210> 337
 <211> 296
 <212> PRT
 <213> E. Coli

Met	Ile	Lys	Lys	Thr	Thr	Glu	Ile	Asp	Ala	Ile	Leu	Leu	Asn	Leu	Asn
1				5					10					15	
Lys	Ala	Ile	Asp	Ala	His	Tyr	Gln	Trp	Leu	Val	Ser	Met	Phe	His	Ser
			20					25					30		
Val	Val	Ala	Arg	Asp	Ala	Ser	Lys	Pro	Glu	Ile	Thr	Asp	Asn	His	Ser
		35					40					45			
Tyr	Gly	Leu	Cys	Gln	Phe	Gly	Arg	Trp	Ile	Asp	His	Leu	Gly	Pro	Leu
50						55					60				
Asp	Asn	Asp	Glu	Leu	Pro	Tyr	Val	Arg	Leu	Met	Asp	Ser	Ala	His	Gln
65					70					75					80

His Met His Asn Cys Gly Arg Glu Leu Met Leu Ala Ile Val Glu Asn
85 90 95
His Trp Gln Asp Ala His Phe Asp Ala Phe Gln Glu Gly Leu Leu Ser
100 105 110
Phe Thr Ala Ala Leu Thr Asp Tyr Lys Ile Tyr Leu Leu Thr Ile Arg
115 120 125
Ser Asn Met Asp Val Leu Thr Gly Leu Pro Gly Arg Arg Val Leu Asp
130 135 140
Glu Ser Phe Asp His Gln Leu Arg Asn Ala Glu Pro Leu Asn Leu Tyr
145 150 155 160
Leu Met Leu Leu Asp Ile Asp Arg Phe Lys Leu Val Asn Asp Thr Tyr
165 170 175
Gly His Leu Ile Gly Asp Val Val Leu Arg Thr Leu Ala Thr Tyr Leu
180 185 190
Ala Ser Trp Thr Arg Asp Tyr Glu Thr Val Tyr Arg Tyr Gly Gly Glu
195 200 205
Glu Phe Ile Ile Ile Val Lys Ala Ala Asn Asp Glu Glu Ala Cys Arg
210 215 220
Ala Gly Val Arg Ile Cys Gln Leu Val Asp Asn His Ala Ile Thr His
225 230 235 240
Ser Glu Gly His Ile Asn Ile Thr Val Thr Ala Gly Val Ser Arg Ala
245 250 255
Phe Pro Glu Glu Pro Leu Asp Val Val Ile Gly Arg Ala Asp Arg Ala
260 265 270
Met Tyr Glu Gly Lys Gln Thr Gly Arg Asn Arg Cys Met Phe Ile Asp
275 280 285
Glu Gln Asn Val Ile Asn Arg Val
290 295

<210> 338
<211> 203
<212> PRT
<213> E. Coli

<400> 338

Met Arg Leu Arg Val Val Pro Gly Phe Ile Ser Pro Pro Pro Gly Phe
1 5 10 15
Gly Gly Leu Gly Tyr Thr Pro Thr Ala Arg Ala Cys Val Asn Ile Ser
20 25 30
Ile Pro Leu Gln Leu Arg Val Ile Asp Met Leu Asp Val Phe Thr Pro
35 40 45
Leu Leu Lys Leu Phe Ala Asn Glu Pro Leu Glu Arg Leu Met Tyr Thr
50 55 60
Ile Ile Ile Phe Gly Leu Thr Leu Trp Leu Ile Pro Lys Glu Phe Thr
65 70 75 80
Val Ala Phe Asn Ala Tyr Thr Glu Ile Pro Trp Leu Phe Gln Ile Ile
85 90 95
Val Phe Ala Phe Ser Phe Val Val Ala Ile Ser Phe Ser Arg Leu Arg
100 105 110
Ala His Ile Gln Lys His Tyr Ser Leu Leu Pro Glu Gln Arg Val Leu
115 120 125
Leu Arg Leu Ser Glu Lys Glu Ile Ala Val Phe Lys Asp Phe Leu Lys
130 135 140
Thr Gly Asn Leu Ile Ile Thr Ser Pro Cys Arg Asn Pro Val Met Lys
145 150 155 160

Leu 210	Thr	Gly	Met	Ala	Asp	Arg 215	Phe	Gly	Arg	Thr	Leu 220	Thr	Tyr	Arg	Arg
Glu 225	Ala	Ala	Gly	Asp	Leu 230	Ala	Gly	Glu	Ile	Thr 235	Gly	Val	Thr	Asp	Gly 240
Ala	Gly	Arg	Glu	Phe 245	Arg	Leu	Val	Leu	Thr 250	Thr	Gln	Ala	Gln	Arg	Ala 255
Glu	Glu	Ala	Arg	Thr 260	Ser	Ser	Leu	Ser	Ser 265	Ser	Asp	Ser	Ser	Arg	Pro
Leu	Ser	Ala	Ser	Ala 275	Phe	Pro	Asp	Thr	Leu 280	Pro	Gly	Thr	Glu	Tyr	Gly
Pro	Asp	Arg	Gly	Ile 290	Arg	Leu	Ser	Ala	Val 295	Trp	Leu 300	Met	His	Asp	Pro
Ala 305	Tyr	Pro	Glu	Ser 310	Leu	Pro	Ala	Ala	Pro 315	Leu	Val	Arg	Tyr	Thr	Tyr 320
Thr	Glu	Ala	Gly	Glu 325	Leu	Leu	Ala	Val	Tyr 330	Asp	Arg	Ser	Asn	Thr	Gln 335
Val	Arg	Ala	Phe 340	Thr	Tyr	Asp	Ala	Gln	His 345	Pro	Gly	Arg	Met	Val	Ala 350
His	Arg	Tyr	Ala 355	Gly	Arg	Pro	Glu	Met	Arg 360	Tyr	Arg	Tyr	Asp	Asp	Thr 365
Gly	Arg	Val	Val 370	Glu	Gln	Leu	Asn	Pro	Ala 375	Gly	Leu 380	Ser	Tyr	Arg	Tyr 385
Leu 385	Tyr	Glu	Gln	Asp 390	Arg	Ile	Thr	Val	Thr 395	Asp	Ser	Leu	Asn	Arg	Arg 400
Glu	Val	Leu	His 405	Thr	Glu	Gly	Gly	Ala	Gly 410	Leu	Lys	Arg	Val	Val	Lys 415
Lys	Glu	Leu	Ala 420	Asp	Gly	Ser	Val	Thr	Arg 425	Ser	Gly	Tyr	Asp	Ala	Ala 430
Gly	Arg	Leu	Thr 435	Ala	Gln	Thr	Asp	Ala	Ala 440	Gly	Arg	Arg	Thr	Glu	Tyr 445
Gly	Leu	Asn	Val 450	Val	Ser	Gly	Asp	Ile	Thr 455	Asp	Ile	Thr	Thr	Pro	Asp 460
Gly 465	Arg	Glu	Thr	Lys 470	Phe	Tyr	Tyr	Asn	Asp 475	Gly	Asn	Gln	Leu	Thr	Ala 480
Val	Val	Ser	Pro 485	Asp	Gly	Leu	Glu	Ser	Arg 490	Arg	Glu	Tyr	Asp	Glu	Pro 495
Gly	Arg	Leu	Val 500	Ser	Glu	Thr	Ser	Arg	Ser 505	Gly	Glu	Thr	Val	Arg	Tyr 510
Arg	Tyr	Asp	Asp 515	Ala	His	Ser	Glu	Leu	Pro 520	Ala	Thr	Thr	Thr	Asp	Ala 525
Thr	Gly	Ser	Thr 530	Arg	Gln	Met	Thr	Trp	Ser 535	Arg	Tyr	Gly	Gln	Leu	Leu 540
Ala 545	Phe	Thr	Asp	Cys 550	Ser	Gly	Tyr	Gln	Thr 555	Arg	Tyr	Glu	Tyr	Asp	Arg 560
Phe	Gly	Gln	Met 565	Thr	Ala	Val	His	Arg	Glu 570	Glu	Gly	Ile	Ser	Leu	Tyr 575
Arg	Arg	Tyr	Asp 580	Asn	Arg	Gly	Arg	Leu	Thr 585	Ser	Val	Lys	Asp	Ala	Gln 590
Gly	Arg	Glu	Thr 595	Arg	Tyr	Glu	Tyr	Asn	Ala 600	Ala	Gly	Asp	Leu	Thr	Ala 605
Val	Ile	Thr	Pro 610	Asp	Gly	Asn	Arg	Ser	Glu 615	Thr	Gln	Tyr	Asp	Ala	Trp 620
Gly 625	Lys	Ala	Val	Ser 630	Thr	Gln	Gly	Gly	Leu 635	Thr	Arg	Ser	Met	Glu	640
Tyr	Asp	Ala	Ala 645	Gly	Arg	Val	Ile	Ser	Leu 650	Thr	Asn	Glu	Asn	Gly	Ser 655
His	Ser	Val	Phe	Ser	Tyr	Asp	Ala	Leu	Asp	Arg	Leu	Val	Gln	Gln	Gly

										660					665					670				
Gly	Phe	Asp	Gly	Arg	Thr	Gln	Arg	Tyr	His	Tyr	Asp	Leu	Thr	Gly	Lys									
		675					680					685												
Leu	Thr	Gln	Ser	Glu	Asp	Glu	Gly	Leu	Val	Ile	Leu	Trp	Tyr	Tyr	Asp									
		690					695					700												
Glu	Ser	Asp	Arg	Ile	Thr	His	Arg	Thr	Val	Asn	Gly	Glu	Pro	Ala	Glu									
		705					710					715												
Gln	Trp	Gln	Tyr	Asp	Gly	His	Gly	Trp	Leu	Thr	Asp	Ile	Ser	His	Leu									
				725							730													
Ser	Glu	Gly	His	Arg	Val	Ala	Val	His	Tyr	Gly	Tyr	Asp	Asp	Lys	Gly									
				740					745															
Arg	Leu	Thr	Gly	Glu	Cys	Gln	Thr	Val	Glu	Asn	Pro	Glu	Thr	Gly	Glu									
				755					760															
Leu	Leu	Trp	Gln	His	Glu	Thr	Lys	His	Ala	Tyr	Asn	Glu	Gln	Gly	Leu									
				770									780											
Ala	Asn	Arg	Val	Thr	Pro	Asp	Ser	Leu	Pro	Pro	Val	Glu	Trp	Leu	Thr									
						790					795													
Tyr	Gly	Ser	Gly	Tyr	Leu	Ala	Gly	Met	Lys	Leu	Gly	Gly	Thr	Pro	Leu									
						805					810													
Val	Glu	Tyr	Thr	Arg	Asp	Arg	Leu	His	Arg	Glu	Thr	Val	Arg	Ser	Phe									
						820					825													
Gly	Ser	Met	Ala	Gly	Ser	Asn	Ala	Ala	Tyr	Glu	Leu	Thr	Ser	Thr	Tyr									
								840																
Thr	Pro	Ala	Gly	Gln	Leu	Gln	Ser	Gln	His	Leu	Asn	Ser	Leu	Val	Tyr									
								855																
Asp	Arg	Asp	Tyr	Gly	Trp	Ser	Asp	Asn	Gly	Asp	Leu	Val	Arg	Ile	Ser									
								870					875											
Gly	Pro	Arg	Gln	Thr	Arg	Glu	Tyr	Gly	Tyr	Ser	Ala	Thr	Gly	Arg	Leu									
										890														
Glu	Ser	Val	Arg	Thr	Leu	Ala	Pro	Asp	Leu	Asp	Ile	Arg	Ile	Pro	Tyr									
										905														
Ala	Thr	Asp	Pro	Ala	Gly	Asn	Arg	Leu	Pro	Asp	Pro	Glu	Leu	His	Pro									
								920					925											
Asp	Ser	Thr	Leu	Thr	Val	Trp	Pro	Asp	Asn	Arg	Ile	Ala	Glu	Asp	Ala									
								935					940											
His	Tyr	Val	Tyr	Arg	His	Asp	Glu	Tyr	Gly	Arg	Leu	Thr	Glu	Lys	Thr									
								950					955											
Asp	Arg	Ile	Pro	Ala	Gly	Val	Ile	Arg	Thr	Asp	Asp	Glu	Arg	Thr	His									
										970														
His	Tyr	His	Tyr	Asp	Ser	Gln	His	Arg	Leu	Val	Phe	Tyr	Thr	Arg	Ile									
										985														
Gln	His	Gly	Glu	Pro	Leu	Val	Glu	Ser	Arg	Tyr	Leu	Tyr	Asp	Pro	Leu									
										1000														
Gly	Arg	Arg	Met	Ala	Lys	Arg	Val	Trp	Arg	Arg	Glu	Arg	Asp	Leu	Thr									
												1020												
Gly	Trp	Met	Ser																					

Arg Val Ser Ser Glu Ser Arg Ala Trp Leu Ala Gln Cys Gly Leu Thr
 1125 1130 1135
 Val Glu Gln Leu Ala Arg Gln Val Glu Pro Glu Tyr Thr Pro Ala Arg
 1140 1145 1150
 Lys Ala His Leu Tyr His Cys Asp His Arg Gly Leu Pro Leu Ala Leu
 1155 1160 1165
 Ile Ser Glu Asp Gly Asn Thr Ala Trp Ser Ala Glu Tyr Asp Glu Trp
 1170 1175 1180
 Gly Asn Gln Leu Asn Glu Glu Asn Pro His His Val Tyr Gln Pro Tyr
 1185 1190 1195 1200
 Arg Leu Pro Gly Gln Gln His Asp Glu Glu Ser Gly Leu Tyr Tyr Asn
 1205 1210 1215
 Arg His Arg Tyr Tyr Asp Pro Leu Gln Gly Arg Tyr Ile Thr Gln Asp
 1220 1225 1230
 Pro Met Gly Leu Lys Gly Gly Trp Asn Leu Tyr Gln Tyr Pro Leu Asn
 1235 1240 1245
 Pro Leu Gln Gln Ile Asp Pro Met Gly Leu Leu Gln Thr Trp Asp Asp
 1250 1255 1260
 Ala Arg Ser Gly Ala Cys Thr Gly Gly Val Cys Gly Val Leu Ser Arg
 1265 1270 1275 1280
 Ile Ile Gly Pro Ser Lys Phe Asp Ser Thr Ala Asp Ala Ala Leu Asp
 1285 1290 1295
 Ala Leu Lys Glu Thr Gln Asn Arg Ser Leu Cys Asn Asp Met Glu Tyr
 1300 1305 1310
 Ser Gly Ile Val Cys Lys Asp Thr Asn Gly Lys Tyr Phe Ala Ser Lys
 1315 1320 1325
 Ala Glu Thr Asp Asn Leu Arg Lys Glu Ser Tyr Pro Leu Lys Arg Lys
 1330 1335 1340
 Cys Pro Thr Gly Thr Asp Arg Val Ala Ala Tyr His Thr His Gly Ala
 1345 1350 1355 1360
 Asp Ser His Gly Asp Tyr Val Asp Glu Phe Phe Ser Ser Ser Asp Lys
 1365 1370 1375
 Asn Leu Val Arg Ser Lys Asp Asn Asn Leu Glu Ala Phe Tyr Leu Ala
 1380 1385 1390
 Thr Pro Asp Gly Arg Phe Glu Ala Leu Asn Asn Lys Gly Glu Tyr Ile
 1395 1400 1405
 Phe Ile Arg Asn Ser Val Pro Gly Leu Ser Ser Val Cys Ile Pro Tyr
 1410 1415 1420
 His Asp
 1425

<210> 341
 <211> 122
 <212> PRT
 <213> E. Coli

<400> 341
 Met Lys Tyr Ser Ser Ile Phe Ser Met Leu Ser Phe Phe Ile Leu Phe
 1 5 10 15
 Ala Cys Asn Glu Thr Ala Val Tyr Gly Ser Asp Glu Asn Ile Ile Phe
 20 25 30
 Met Arg Tyr Val Glu Lys Leu His Leu Asp Lys Tyr Ser Val Lys Asn
 35 40 45
 Thr Val Lys Thr Glu Thr Met Ala Ile Gln Leu Ala Glu Ile Tyr Val
 50 55 60
 Arg Tyr Arg Tyr Gly Glu Arg Ile Ala Glu Glu Glu Lys Pro Tyr Leu

65					70					75				80	
Ile	Thr	Glu	Leu	Pro	Asp	Ser	Trp	Val	Val	Glu	Gly	Ala	Lys	Leu	Pro
				85					90					95	
Tyr	Glu	Val	Ala	Gly	Gly	Val	Phe	Ile	Ile	Glu	Ile	Asn	Lys	Lys	Asn
			100					105					110		
Gly	Cys	Val	Leu	Asn	Phe	Leu	His	Ser	Lys						
		115					120								

<210> 342
 <211> 236
 <212> PRT
 <213> E. Coli

<400> 342

Met	Leu	Ala	Leu	Met	Asp	Ala	Asp	Gly	Asn	Ile	Ala	Trp	Ser	Gly	Glu
1				5					10					15	
Tyr	Asp	Glu	Trp	Gly	Asn	Gln	Leu	Asn	Glu	Glu	Asn	Pro	His	His	Leu
			20					25				30			
His	Gln	Pro	Tyr	Arg	Leu	Pro	Gly	Gln	Gln	Tyr	Asp	Lys	Glu	Ser	Gly
		35					40					45			
Leu	Tyr	Tyr	Asn	Arg	Asn	Arg	Tyr	Tyr	Asp	Pro	Leu	Gln	Gly	Arg	Tyr
		50				55					60				
Ile	Thr	Gln	Asp	Pro	Ile	Gly	Leu	Glu	Gly	Gly	Trp	Ser	Leu	Tyr	Ala
65					70				75						80
Tyr	Pro	Leu	Asn	Pro	Val	Asn	Gly	Ile	Asp	Pro	Leu	Gly	Leu	Ser	Pro
			85					90						95	
Ala	Asp	Val	Ala	Leu	Ile	Arg	Arg	Lys	Asp	Gln	Leu	Asn	His	Gln	Arg
			100					105					110		
Ala	Trp	Asp	Ile	Leu	Ser	Asp	Thr	Tyr	Glu	Asp	Met	Lys	Arg	Leu	Asn
		115					120					125			
Leu	Gly	Gly	Thr	Asp	Gln	Phe	Phe	His	Cys	Met	Ala	Phe	Cys	Arg	Val
		130				135					140				
Ser	Lys	Leu	Asn	Asp	Ala	Gly	Val	Ser	Arg	Ser	Ala	Lys	Gly	Leu	Gly
145					150					155					160
Tyr	Glu	Lys	Glu	Ile	Arg	Asp	Tyr	Gly	Leu	Asn	Leu	Phe	Gly	Met	Tyr
			165					170						175	
Gly	Arg	Lys	Val	Lys	Leu	Ser	His	Ser	Glu	Met	Ile	Glu	Asp	Asn	Lys
			180					185					190		
Lys	Asp	Leu	Ala	Val	Asn	Asp	His	Gly	Leu	Thr	Cys	Pro	Ser	Thr	Thr
		195					200					205			
Asp	Cys	Ser	Asp	Arg	Cys	Ser	Asp	Tyr	Ile	Asn	Pro	Glu	His	Lys	Lys
	210					215					220				
Thr	Ile	Lys	Ala	Leu	Gln	Asp	Ala	Gly	Tyr	Leu	Lys				
225					230					235					

<210> 343
 <211> 86
 <212> PRT
 <213> E. Coli

<400> 343

Met	Leu	Ala	Ile	Ser	Ser	Asn	Leu	Ser	Lys	Met	Ile	Ile	Phe	Ile	Phe
1				5					10					15	
Ala	Ile	Ile	Ile	Ile	Val	Val	Leu	Cys	Val	Ile	Thr	Tyr	Leu	Tyr	Leu
			20					25					30		

Tyr Lys Asp Glu Ser Leu Val Ser Lys His Tyr Ile Asn Tyr Met Ala
 35 40 45
 Ile Pro Glu Asn Asp Gly Val Phe Thr Trp Leu Pro Asp Phe Phe Pro
 50 55 60
 His Val Ala Val Asp Ile Ser Ile Tyr Thr Asn Val Glu Asp Asp Tyr
 65 70 75 80
 Phe Phe Leu Ile Phe Pro
 85

<210> 344
 <211> 63
 <212> PRT
 <213> E. Coli

<400> 344
 Met Arg Ala Arg Glu Gln Val Ala Lys Ile Val Ser Lys Asn Asp Pro
 1 5 10 15
 Asp Thr Lys Lys Val Trp Cys Lys Tyr Gly Lys Ile Pro Gly Gln Gly
 20 25 30
 Asp Gly Val Asn Leu Phe Phe Val Gly Glu Ile Asn Val Thr His Tyr
 35 40 45
 Phe Ile Thr Asn Ile Gly Ala Gly Leu Pro Asp Ala Cys Ala Glu
 50 55 60

<210> 345
 <211> 167
 <212> PRT
 <213> E. Coli

<400> 345
 Met Pro Gly Asn Ser Pro His Tyr Gly Arg Trp Pro Gln His Asp Phe
 1 5 10 15
 Thr Ser Leu Lys Lys Leu Arg Pro Gln Ser Val Thr Ser Arg Ile Gln
 20 25 30
 Pro Gly Ser Asp Val Ile Val Cys Ala Glu Met Asp Glu Gln Trp Gly
 35 40 45
 Tyr Val Gly Ala Lys Ser Arg Gln Arg Trp Leu Phe Tyr Ala Tyr Asp
 50 55 60
 Ser Leu Arg Lys Thr Val Val Ala His Val Phe Gly Glu Arg Thr Met
 65 70 75 80
 Ala Thr Leu Gly Arg Leu Met Ser Leu Leu Ser Pro Phe Asp Val Val
 85 90 95
 Ile Trp Met Thr Asp Gly Trp Pro Leu Tyr Glu Ser Arg Leu Lys Gly
 100 105 110
 Lys Leu His Val Ile Ser Lys Arg Tyr Thr Gln Arg Ile Glu Arg His
 115 120 125
 Asn Leu Asn Leu Arg Gln His Leu Ala Arg Leu Gly Arg Lys Ser Leu
 130 135 140
 Ser Phe Ser Lys Ser Val Glu Leu His Asp Lys Val Ile Gly His Tyr
 145 150 155 160
 Leu Asn Ile Lys His Tyr Gln
 165

<210> 346
 <211> 91
 <212> PRT
 <213> E. Coli

<400> 346
 Met Ala Ser Val Ser Ile Ser Cys Pro Ser Cys Ser Ala Thr Asp Gly
 1 5 10 15
 Val Val Arg Asn Gly Lys Ser Thr Ala Gly His Gln Arg Tyr Leu Cys
 20 25 30
 Ser His Cys Arg Lys Thr Trp Gln Leu Gln Phe Thr Tyr Thr Ala Ser
 35 40 45
 Gln Pro Gly Thr His Gln Lys Ile Ile Asp Met Ala Met Asn Gly Val
 50 55 60
 Gly Cys Arg Ala Thr Ala Arg Ile Met Gly Val Gly Leu Asn Thr Ile
 65 70 75 80
 Leu Arg His Leu Lys Asn Ser Gly Arg Ser Arg
 85 90

<210> 347
 <211> 138
 <212> PRT
 <213> E. Coli

<400> 347
 Met Met Thr Lys Thr Gln Ile Asn Lys Leu Ile Lys Met Met Asn Asp
 1 5 10 15
 Leu Asp Tyr Pro Phe Glu Ala Pro Leu Lys Glu Ser Phe Ile Glu Ser
 20 25 30
 Ile Ile Gln Ile Glu Phe Asn Ser Asn Ser Thr Asn Cys Leu Glu Lys
 35 40 45
 Leu Cys Asn Glu Val Ser Ile Leu Phe Lys Asn Gln Pro Asp Tyr Leu
 50 55 60
 Thr Phe Leu Arg Ala Met Asp Gly Phe Glu Val Asn Gly Leu Arg Leu
 65 70 75 80
 Phe Ser Leu Ser Ile Pro Glu Pro Ser Val Lys Asn Leu Phe Ala Val
 85 90 95
 Asn Glu Phe Tyr Arg Asn Asn Asp Asp Phe Ile Asn Pro Asp Leu Gln
 100 105 110
 Glu Arg Leu Val Ile Gly Asp Tyr Ser Ile Ser Ile Phe Thr Tyr Asp
 115 120 125
 Ile Lys Gly Asp Ala Ala Asn Leu Leu Ile
 130 135

<210> 348
 <211> 392
 <212> PRT
 <213> E. Coli

<400> 348
 Met Ser Asn Ile Val Tyr Leu Thr Val Thr Gly Glu Gln Gln Gly Ser
 1 5 10 15
 Ile Ser Ala Gly Cys Gly Thr Ser Glu Ser Thr Gly Asn Arg Trp Gln

002210-60226460

				20				25					30		
Ser	Gly	His	Glu	Asp	Glu	Ile	Phe	Thr	Phe	Ser	Leu	Leu	Asn	Asn	Ile
		35					40					45			
Asn	Asn	Thr	Gly	Leu	Gly	Ser	Gln	Phe	His	Gly	Ile	Thr	Phe	Cys	Lys
	50					55					60				
Leu	Ile	Asp	Lys	Ser	Thr	Pro	Leu	Phe	Ile	Asn	Ser	Ile	Asn	Asn	Asn
65					70					75					80
Glu	Gln	Leu	Phe	Met	Gly	Phe	Asp	Phe	Tyr	Arg	Ile	Asn	Arg	Phe	Gly
				85					90					95	
Arg	Leu	Glu	Lys	Tyr	Tyr	Tyr	Ile	Gln	Leu	Arg	Gly	Ala	Phe	Leu	Ser
			100					105					110		
Ala	Ile	His	His	Gln	Ile	Ile	Glu	Asn	Gln	Leu	Asp	Thr	Glu	Thr	Ile
		115					120					125			
Thr	Ile	Ser	Tyr	Glu	Phe	Ile	Leu	Cys	Gln	His	Leu	Ile	Ala	Asn	Thr
	130					135					140				
Glu	Phe	Ser	Tyr	Leu	Ala	Leu	Pro	Glu	Asn	Tyr	Asn	Arg	Leu	Phe	Leu
145					150					155					160
Pro	Asn	Ser	Lys	Asn	Gln	Thr	Asn	Asn	Arg	Phe	Lys	Thr	Leu	Asn	Ser
				165					170					175	
Lys	Ala	Ile	Gly	Arg	Leu	Leu	Ala	Ala	Gly	Gly	Val	Tyr	Asn	Gly	Asn
			180					185					190		
Ile	Glu	Gly	Phe	Arg	Asp	Thr	Ala	Glu	Lys	Leu	Gly	Gly	Asp	Ala	Ile
		195					200					205			
Lys	Gly	Tyr	Asp	Gln	Ile	Leu	Asn	Glu	Lys	Thr	Ala	Gly	Ile	Ala	Ile
	210					215					220				
Ala	Thr	Ala	Ser	Ile	Leu	Leu	Thr	Lys	Arg	Ser	Asn	Val	Asp	Thr	Tyr
225					230					235					240
Thr	Glu	Ile	Asn	Ser	Tyr	Leu	Gly	Lys	Leu	Arg	Gly	Gln	Gln	Lys	Leu
				245					250					255	
Leu	Asp	Gly	Ile	Asp	Ile	Ile	Glu	Ile	Ile	Tyr	Ile	Lys	Arg	Pro	Ser
			260					265					270		
Lys	Asp	Leu	Ala	Asn	Leu	Arg	Lys	Glu	Phe	Asn	Lys	Thr	Val	Arg	Lys
		275					280					285			
Asn	Phe	Leu	Ile	Lys	Leu	Ala	Lys	Thr	Ser	Glu	Ala	Ser	Gly	Arg	Phe
	290					295					300				
Asn	Ala	Glu	Asp	Leu	Leu	Arg	Met	Arg	Lys	Gly	Asn	Val	Pro	Leu	Asn
305					310					315					320
Tyr	Asn	Val	His	His	Lys	Leu	Ser	Leu	Asp	Asp	Gly	Gly	Thr	Asn	Asp
				325					330					335	
Phe	Glu	Asn	Leu	Val	Leu	Ile	Glu	Asn	Glu	Pro	Tyr	His	Lys	Val	Phe
			340					345					350		
Thr	Asn	Met	Gln	Ser	Arg	Ile	Ala	Lys	Gly	Ile	Leu	Val	Gly	Glu	Ser
		355					360					365			
Lys	Ile	Thr	Pro	Trp	Ala	Ile	Pro	Ser	Gly	Ser	Ile	Tyr	Pro	Pro	Met
	370														

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<210> 349
<211> 221
<212> PRT
<213> E. Coli
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<400> 349
Met Val Leu Ala Leu Asn Tyr Asn Met His Gly Val Asn Ile Arg Ser

1	5	10	15
Glu Asn Ala Ala Lys Pro His Thr Met Pro Ser Arg Tyr Leu Cys Glu			
	20	25	30
Tyr Ile Arg Ser Ile Glu Lys Asn Gly His Ala Leu Asp Phe Gly Cys			
	35	40	45
Gly Lys Leu Arg Tyr Ser Asp Glu Leu Ile Ser Lys Phe Asp Glu Val			
	50	55	60
Thr Phe Leu Asp Ser Lys Arg Gln Leu Glu Arg Glu Gln Ile Ile Arg			
65	70	75	80
Gly Ile Lys Thr Lys Ile Ile Asp Tyr Val Pro Arg Tyr Tyr Lys Asn			
	85	90	95
Ala Asn Thr Val Ala Phe Glu Asp Val Asp Lys Ile Ile Gly Gly Tyr			
	100	105	110
Asp Phe Ile Leu Cys Ser Asn Val Leu Ser Ala Val Pro Cys Arg Asp			
	115	120	125
Thr Ile Asp Lys Ile Val Leu Ser Ile Lys Arg Leu Leu Lys Ser Gly			
	130	135	140
Gly Glu Thr Leu Ile Val Asn Gln Tyr Lys Ser Ser Tyr Phe Lys Lys			
145	150	155	160
Tyr Glu Thr Gly Arg Lys His Leu Tyr Gly Tyr Ile Tyr Lys Asn Ser			
	165	170	175
Lys Ser Val Ser Tyr Tyr Gly Leu Leu Asp Glu Leu Ala Val Gln Glu			
	180	185	190
Ile Cys Ser Ser His Gly Leu Glu Ile Leu Lys Ser Trp Ser Lys Ala			
	195	200	205
Gly Ser Ser Tyr Val Thr Val Gly Ser Cys Asn Ala Ile			
	210	215	220

<210> 350
 <211> 234
 <212> PRT
 <213> E. Coli

<400> 350

Met Asn Asn Met Phe Glu Pro Pro Lys Asn Tyr Asn Glu Met Leu Pro	
1	5
Lys Leu His Lys Ala Thr Phe Leu Asn Thr Leu Ile Tyr Cys Ile Leu	
	20
Leu Val Ile Tyr Glu Tyr Ile Pro Leu Ile Thr Leu Pro Thr Lys Tyr	
	35
Val Pro Pro Ile Lys Asp His Glu Ser Phe Ile Asn Trp Ala Leu Ser	
	50
Phe Gly Ile Leu Pro Cys Ala Phe Ala Ile Phe Ala Tyr Leu Ile Ser	
65	70
Gly Ala Leu Asp Leu His Asn Asn Ala Ala Lys Leu Leu Arg Val Arg	
	85
Tyr Leu Trp Asp Lys His Leu Ile Ile Lys Pro Leu Ser Arg Arg Ala	
	100
Gly Val Asn Arg Lys Leu Asn Lys Asp Glu Ala His Asn Val Met Ser	
	115
Asn Leu Tyr Tyr Pro Glu Val Arg Lys Ile Glu Asp Lys His Tyr Ile	
	130
Glu Leu Phe Trp Asn Lys Val Tyr Tyr Phe Trp Ile Phe Phe Glu Phe	
145	150
Ser Ile Ile Ala Leu Ile Ser Phe Leu Ile Ile Phe Phe Cys Lys Gln	
	165
	170
	175

Met Asp Ile Phe His Val Glu Gly Ser Leu Leu Ser Leu Phe Phe Phe
 180 185 190
 Val Ile Leu Ser Phe Ser Val Ser Gly Ile Ile Phe Ala Leu Thr Val
 195 200 205
 Lys Pro Arg Thr Glu Ser Gln Val Gly Lys Ile Pro Asp Asp Lys Ile
 210 215 220
 Lys Glu Phe Phe Thr Lys Asn Asn Ile Asn
 225 230

<210> 351
 <211> 94
 <212> PRT
 <213> E. Coli

<400> 351
 Met Phe Thr Ile Asn Ala Glu Val Arg Lys Glu Gln Gly Lys Gly Ala
 1 5 10 15
 Ser Arg Arg Leu Arg Ala Ala Asn Lys Phe Pro Ala Ile Ile Tyr Gly
 20 25 30
 Gly Lys Glu Ala Pro Leu Ala Ile Glu Leu Asp His Asp Lys Val Met
 35 40 45
 Asn Met Gln Ala Lys Ala Glu Phe Tyr Ser Glu Val Leu Thr Ile Val
 50 55 60
 Val Asp Gly Lys Glu Ile Lys Val Lys Ala Gln Asp Val Gln Arg His
 65 70 75 80
 Pro Tyr Lys Pro Lys Leu Gln His Ile Asp Phe Val Arg Ala
 85 90

<210> 352
 <211> 658
 <212> PRT
 <213> E. Coli

<400> 352
 Met Val Leu Phe Tyr Arg Ala His Trp Arg Asp Tyr Lys Asn Asp Gln
 1 5 10 15
 Val Arg Ile Met Met Asn Leu Thr Thr Leu Thr His Arg Asp Ala Leu
 20 25 30
 Cys Leu Asn Ala Arg Phe Thr Ser Arg Glu Glu Ala Ile His Ala Leu
 35 40 45
 Thr Gln Arg Leu Ala Ala Leu Gly Lys Ile Ser Ser Thr Glu Gln Phe
 50 55 60
 Leu Glu Glu Val Tyr Arg Glu Ser Leu Gly Pro Thr Ala Leu Gly
 65 70 75 80
 Glu Gly Leu Ala Val Pro His Gly Lys Thr Ala Ala Val Lys Glu Ala
 85 90 95
 Ala Phe Ala Val Ala Thr Leu Ser Glu Pro Leu Gln Trp Glu Gly Val
 100 105 110
 Asp Gly Pro Glu Ala Val Asp Leu Val Val Leu Leu Ala Ile Pro Pro
 115 120 125
 Asn Glu Ala Gly Thr Thr His Met Gln Leu Leu Thr Ala Leu Thr Thr
 130 135 140
 Arg Leu Ala Asp Asp Glu Ile Arg Ala Arg Ile Gln Ser Ala Thr Thr
 145 150 155 160

Pro Asp Glu Leu Leu Ser Ala Leu Asp Asp Lys Gly Gly Thr Gln Pro
 165 170 175
 Ser Ala Ser Phe Ser Asn Ala Pro Thr Ile Val Cys Val Thr Ala Cys
 180 185 190
 Pro Ala Gly Ile Ala His Thr Tyr Met Ala Ala Glu Tyr Leu Glu Lys
 195 200 205
 Ala Gly Arg Lys Leu Gly Val Asn Val Tyr Val Glu Lys Gln Gly Ala
 210 215 220
 Asn Gly Ile Glu Gly Arg Leu Thr Ala Asp Gln Leu Asn Ser Ala Thr
 225 230 235 240
 Ala Cys Ile Phe Ala Ala Glu Val Ala Ile Lys Glu Ser Glu Arg Phe
 245 250 255
 Asn Gly Ile Pro Ala Leu Ser Val Pro Val Ala Glu Pro Ile Arg His
 260 265 270
 Ala Glu Ala Leu Ile Gln Gln Ala Leu Thr Leu Lys Arg Ser Asp Glu
 275 280 285
 Thr Arg Thr Val Gln Gln Asp Thr Gln Pro Val Lys Ser Val Lys Thr
 290 295 300
 Glu Leu Lys Gln Ala Leu Leu Ser Gly Ile Ser Phe Ala Val Pro Leu
 305 310 315 320
 Ile Val Ala Gly Gly Thr Val Leu Ala Val Ala Val Leu Leu Ser Gln
 325 330 335
 Ile Phe Gly Leu Gln Asp Leu Phe Asn Glu Glu Asn Ser Trp Leu Trp
 340 345 350
 Met Tyr Arg Lys Leu Gly Gly Gly Leu Leu Gly Ile Leu Met Val Pro
 355 360 365
 Val Leu Ala Ala Tyr Thr Ala Tyr Ser Leu Ala Asp Lys Pro Ala Leu
 370 375 380
 Ala Pro Gly Phe Ala Ala Gly Leu Ala Ala Asn Met Ile Gly Ser Gly
 385 390 395 400
 Phe Leu Gly Ala Val Val Gly Gly Leu Ile Ala Gly Tyr Leu Met Arg
 405 410 415
 Trp Val Lys Asn His Leu Arg Leu Ser Ser Lys Phe Asn Gly Phe Leu
 420 425 430
 Thr Phe Tyr Leu Tyr Pro Val Leu Gly Thr Leu Gly Ala Gly Ser Leu
 435 440 445
 Met Leu Phe Val Val Gly Glu Pro Val Ala Trp Ile Asn Asn Ser Leu
 450 455 460
 Thr Ala Trp Leu Asn Gly Leu Ser Gly Ser Asn Ala Leu Leu Leu Gly
 465 470 475 480
 Ala Ile Leu Gly Phe Met Cys Ser Phe Asp Leu Gly Gly Pro Val Asn
 485 490 495
 Lys Ala Ala Tyr Ala Phe Cys Leu Gly Ala Met Ala Asn Gly Val Tyr
 500 505 510
 Gly Pro Tyr Ala Ile Phe Ala Ser Val Lys Met Val Ser Ala Phe Thr
 515 520 525
 Val Thr Ala Ser Thr Met Leu Ala Pro Arg Leu Phe Lys Glu Phe Glu
 530 535 540
 Ile Glu Thr Gly Lys Ser Thr Trp Leu Leu Gly Leu Ala Gly Ile Thr
 545 550 555 560
 Glu Gly Ala Ile Pro Met Ala Ile Glu Asp Pro Leu Arg Val Ile Gly
 565 570 575
 Ser Phe Val Leu Gly Ser Met Val Thr Gly Ala Ile Val Gly Ala Met
 580 585 590
 Asn Ile Gly Leu Ser Thr Pro Gly Ala Gly Ile Phe Ser Leu Phe Leu
 595 600 605
 Leu His Asp Asn Gly Ala Gly Gly Val Met Ala Ala Ile Gly Trp Phe

610 615 620
 Gly Ala Ala Leu Val Gly Ala Ala Ile Ser Thr Ala Ile Leu Leu Met
 625 630 635 640
 Trp Arg Arg His Ala Val Lys His Gly Asn Tyr Leu Thr Asp Gly Val
 645 650 655
 Met Pro

<210> 353
 <211> 877
 <212> PRT
 <213> E. Coli

<400> 353
 Met Lys Ala Val Ser Arg Val His Ile Thr Pro His Met His Trp Asp
 1 5 10 15
 Arg Glu Trp Tyr Phe Thr Thr Glu Glu Ser Arg Ile Leu Leu Val Asn
 20 25 30
 Asn Met Glu Glu Ile Leu Cys Arg Leu Glu Gln Asp Asn Glu Tyr Lys
 35 40 45
 Tyr Tyr Val Leu Asp Gly Gln Thr Ala Ile Leu Glu Asp Tyr Phe Ala
 50 55 60
 Val Lys Pro Glu Asn Lys Asp Arg Val Lys Lys Gln Val Glu Ala Gly
 65 70 75 80
 Lys Leu Ile Ile Gly Pro Trp Tyr Thr Gln Thr Asp Thr Thr Ile Val
 85 90 95
 Ser Ala Glu Ser Ile Val Arg Asn Leu Met Tyr Gly Met Arg Asp Cys
 100 105 110
 Leu Ala Phe Gly Glu Pro Met Lys Ile Gly Tyr Leu Pro Asp Ser Phe
 115 120 125
 Gly Met Ser Gly Gln Leu Pro His Ile Tyr Asn Gly Phe Gly Ile Thr
 130 135 140
 Arg Thr Met Phe Trp Arg Gly Cys Ser Glu Arg His Gly Thr Asp Lys
 145 150 155 160
 Thr Glu Phe Leu Trp Gln Ser Ser Asp Gly Ser Glu Val Thr Ala Gln
 165 170 175
 Val Leu Pro Leu Gly Tyr Ala Ile Gly Lys Tyr Leu Pro Ala Asp Glu
 180 185 190
 Asn Gly Leu Arg Lys Arg Leu Asp Ser Tyr Phe Asp Val Leu Glu Lys
 195 200 205
 Ala Ser Val Thr Lys Glu Ile Leu Leu Pro Asn Gly His Asp Gln Met
 210 215 220
 Pro Leu Gln Gln Asn Ile Phe Glu Val Met Asp Lys Leu Arg Glu Ile
 225 230 235 240
 Tyr Pro Gln Arg Lys Phe Val Met Ser Arg Phe Glu Glu Val Phe Glu
 245 250 255
 Lys Ile Glu Ala Gln Arg Asp Asn Leu Ala Thr Leu Lys Gly Glu Phe
 260 265 270
 Ile Asp Gly Lys Tyr Met Arg Val His Arg Thr Ile Gly Ser Thr Arg
 275 280 285
 Met Asp Ile Lys Ile Ala His Ala Arg Ile Glu Asn Lys Ile Val Asn
 290 295 300
 Leu Leu Glu Pro Leu Ala Thr Leu Ala Trp Thr Leu Gly Phe Glu Tyr
 305 310 315 320
 His His Gly Leu Leu Glu Lys Met Trp Lys Glu Ile Leu Lys Asn His
 325 330 335

Ala	His	Asp	Ser	Ile	Gly	Cys	Cys	Cys	Ser	Asp	Lys	Val	His	Arg	Glu
			340					345					350		
Ile	Val	Ala	Arg	Phe	Glu	Leu	Ala	Glu	Asp	Met	Ala	Asp	Asn	Leu	Ile
		355					360					365			
Arg	Phe	Tyr	Met	Arg	Lys	Ile	Ala	Asp	Asn	Met	Pro	Gln	Ser	Asp	Ala
	370				375				380						
Asp	Lys	Leu	Val	Leu	Phe	Asn	Leu	Met	Pro	Trp	Pro	Arg	Glu	Glu	Val
385				390					395						400
Ile	Asn	Thr	Thr	Val	Arg	Leu	Arg	Ala	Ser	Gln	Phe	Asn	Leu	Arg	Asp
			405					410						415	
Asp	Arg	Gly	Gln	Pro	Val	Pro	Tyr	Phe	Ile	Arg	His	Ala	Arg	Glu	Ile
		420						425				430			
Asp	Pro	Gly	Leu	Ile	Asp	Arg	Gln	Ile	Val	His	Tyr	Gly	Asn	Tyr	Asp
		435					440					445			
Pro	Phe	Met	Glu	Phe	Asp	Ile	Gln	Ile	Asn	Gln	Ile	Val	Pro	Ser	Met
	450				455						460				
Gly	Tyr	Arg	Thr	Leu	Tyr	Ile	Glu	Ala	Asn	Gln	Pro	Gly	Asn	Val	Ile
465				470						475					480
Ala	Ala	Lys	Ser	Asp	Ala	Glu	Gly	Ile	Leu	Glu	Asn	Ala	Phe	Trp	Gln
			485					490					495		
Ile	Ala	Leu	Asn	Glu	Asp	Gly	Ser	Leu	Gln	Leu	Val	Asp	Lys	Asp	Ser
			500					505				510			
Gly	Val	Arg	Tyr	Asp	Arg	Val	Leu	Gln	Ile	Glu	Glu	Ser	Ser	Asp	Asp
		515				520						525			
Gly	Asp	Glu	Tyr	Asp	Tyr	Ser	Pro	Ala	Lys	Glu	Glu	Trp	Val	Ile	Thr
	530				535						540				
Ala	Ala	Asn	Ala	Lys	Pro	Gln	Cys	Asp	Ile	Ile	His	Glu	Ala	Trp	Gln
545				550					555						560
Ser	Arg	Ala	Val	Ile	Arg	Tyr	Asp	Met	Ala	Val	Pro	Leu	Asn	Leu	Ser
			565					570						575	
Glu	Arg	Ser	Ala	Arg	Gln	Ser	Thr	Gly	Arg	Val	Gly	Val	Val	Leu	Val
		580						585				590			
Val	Thr	Leu	Ser	His	Asn	Ser	Arg	Arg	Ile	Asp	Val	Asp	Ile	Asn	Leu
		595				600						605			
Asp	Asn	Gln	Ala	Asp	Asp	His	Arg	Leu	Arg	Val	Leu	Val	Pro	Thr	Pro
	610				615						620				
Phe	Asn	Thr	Asp	Ser	Val	Leu	Ala	Asp	Thr	Gln	Phe	Gly	Ser	Leu	Thr
625				630					635						640
Arg	Pro	Val	Asn	Asp	Ser	Ala	Met	Asn	Asn	Trp	Gln	Gln	Glu	Gly	Trp
			645					650						655	
Lys	Glu	Ala	Pro	Val	Pro	Val	Trp	Asn	Met	Leu	Asn	Tyr	Val	Ala	Leu
		660						665				670			
Gln	Glu	Gly	Arg	Asn	Gly	Met	Ala	Val	Phe	Ser	Glu	Gly	Leu	Arg	Glu
		675				680						685			
Phe	Glu	Val	Ile	Gly	Glu	Glu	Lys	Lys	Thr	Phe	Ala	Ile	Thr	Leu	Leu
	690				695					700					
Arg	Gly	Val	Gly	Leu	Leu	Gly	Lys	Glu	Asp	Leu	Leu	Leu	Arg	Pro	Gly
705				710					715						720
Arg	Pro	Ser	Gly	Ile	Lys	Met	Pro	Val	Pro	Asp	Ser	Gln	Leu	Arg	Gly
			725					730						735	
Leu	Leu	Ser	Cys	Arg	Leu	Ser	Leu	Leu	Ser	Tyr	Thr	Gly	Thr	Pro	Thr
		740					745					750			
Ala	Ala	Gly	Val	Ala	Gln	Gln	Ala	Arg	Ala	Trp	Leu	Thr	Pro	Val	Gln
		755				760					765				
Cys	Tyr	Asn	Lys	Ile	Pro	Trp	Asp	Val	Met	Lys	Leu	Asn	Lys	Ala	Gly
	770				775						780				
Phe	Asn	Val	Pro	Glu	Ser	Tyr	Ser	Leu	Leu	Lys	Met	Pro	Pro	Val	Gly

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785          790          795          800
Cys Leu Ile Ser Ala Leu Lys Lys Ala Glu Asp Arg Gln Glu Val Ile
      805          810          815
Leu Arg Leu Phe Asn Pro Ala Glu Ser Ala Thr Cys Asp Ala Thr Val
      820          825          830
Ala Phe Ser Arg Glu Val Ile Ser Cys Ser Glu Thr Met Met Asp Glu
      835          840          845
His Ile Thr Thr Glu Glu Asn Gln Gly Ser Asn Leu Ser Gly Pro Phe
      850          855          860
Leu Pro Gly Gln Ser Arg Thr Phe Ser Tyr Arg Leu Ala
865          870          875

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<210> 354
<211> 523
<212> PRT
<213> E. Coli

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<400> 354
Met Met Leu Asp Ile Val Glu Leu Ser Arg Leu Gln Phe Ala Leu Thr
 1          5          10          15
Ala Met Tyr His Phe Leu Phe Val Pro Leu Thr Leu Gly Met Ala Phe
 20          25          30
Leu Leu Ala Ile Met Glu Thr Val Tyr Val Leu Ser Gly Lys Gln Ile
 35          40          45
Tyr Lys Asp Met Thr Lys Phe Trp Gly Lys Leu Phe Gly Ile Asn Phe
 50          55          60
Ala Leu Gly Val Ala Thr Gly Leu Thr Met Glu Phe Gln Phe Gly Thr
 65          70          75          80
Asn Trp Ser Tyr Tyr Ser His Tyr Val Gly Asp Ile Phe Gly Ala Pro
      85          90          95
Leu Ala Ile Glu Gly Leu Met Ala Phe Phe Leu Glu Ser Thr Phe Val
      100          105          110
Gly Leu Phe Phe Phe Gly Trp Asp Arg Leu Gly Lys Val Gln His Met
      115          120          125
Cys Val Thr Trp Leu Val Ala Leu Gly Ser Asn Leu Ser Ala Leu Trp
      130          135          140
Ile Leu Val Ala Asn Gly Trp Met Gln Asn Pro Ile Ala Ser Asp Phe
      145          150          155          160
Asn Phe Glu Thr Met Arg Met Glu Met Val Ser Phe Ser Glu Leu Val
      165          170          175
Leu Asn Pro Val Ala Gln Val Lys Phe Val His Thr Val Ala Ser Gly
      180          185          190
Tyr Val Thr Gly Ala Met Phe Ile Leu Gly Ile Ser Ala Trp Tyr Met
      195          200          205
Leu Lys Gly Arg Asp Phe Ala Phe Ala Lys Arg Ser Phe Ala Ile Ala
      210          215          220
Ala Ser Phe Gly Met Ala Ala Val Leu Ser Val Ile Val Leu Gly Asp
      225          230          235          240
Glu Ser Gly Tyr Glu Met Gly Asp Val Gln Lys Thr Lys Leu Ala Ala
      245          250          255
Ile Glu Ala Glu Trp Glu Thr Gln Pro Ala Pro Ala Ala Phe Thr Leu
      260          265          270
Phe Gly Ile Pro Asp Gln Glu Glu Glu Thr Asn Lys Phe Ala Ile Gln
      275          280          285
Ile Pro Tyr Ala Leu Gly Ile Ile Ala Thr Arg Ser Val Asp Thr Pro
      290          295          300

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Val Ile Gly Leu Lys Glu Leu Met Val Gln His Glu Glu Arg Ile Arg
 305 310 315 320
 Asn Gly Met Lys Ala Tyr Ser Leu Leu Glu Gln Leu Arg Ser Gly Ser
 325 330 335
 Thr Asp Gln Ala Val Arg Asp Gln Phe Asn Ser Met Lys Lys Asp Leu
 340 345 350
 Gly Tyr Gly Leu Leu Leu Lys Arg Tyr Thr Pro Asn Val Ala Asp Ala
 355 360 365
 Thr Glu Ala Gln Ile Gln Gln Ala Thr Lys Asp Ser Ile Pro Arg Val
 370 375 380
 Ala Pro Leu Tyr Phe Ala Phe Arg Ile Met Val Ala Cys Gly Phe Leu
 385 390 395 400
 Leu Leu Ala Ile Ile Ala Leu Ser Phe Trp Ser Val Ile Arg Asn Arg
 405 410 415
 Ile Gly Glu Lys Lys Trp Leu Leu Arg Ala Ala Leu Tyr Gly Ile Pro
 420 425 430
 Leu Pro Trp Ile Ala Val Glu Ala Gly Trp Phe Val Ala Glu Tyr Gly
 435 440 445
 Arg Gln Pro Trp Ala Ile Gly Glu Val Leu Pro Thr Ala Val Ala Asn
 450 455 460
 Ser Ser Leu Thr Ala Gly Asp Leu Ile Phe Ser Met Val Leu Ile Cys
 465 470 475 480
 Gly Leu Tyr Thr Leu Phe Leu Val Ala Glu Leu Phe Leu Met Phe Lys
 485 490 495
 Phe Ala Arg Leu Gly Pro Ser Ser Leu Lys Thr Gly Arg Tyr His Phe
 500 505 510
 Glu Gln Ser Thr Thr Thr Gln Pro Ala Arg
 515 520

<210> 355
 <211> 379
 <212> PRT
 <213> E. Coli

<400> 355
 Met Ile Asp Tyr Glu Val Leu Arg Phe Ile Trp Trp Leu Leu Val Gly
 1 5 10 15
 Val Leu Leu Ile Gly Phe Ala Val Thr Asp Gly Phe Asp Met Gly Val
 20 25 30
 Gly Met Leu Thr Arg Phe Leu Gly Arg Asn Asp Thr Glu Arg Arg Ile
 35 40 45
 Met Ile Asn Ser Ile Ala Pro His Trp Asp Gly Asn Gln Val Trp Leu
 50 55 60
 Ile Thr Ala Gly Gly Ala Leu Phe Ala Ala Trp Pro Met Val Tyr Ala
 65 70 75 80
 Ala Ala Phe Ser Gly Phe Tyr Val Ala Met Ile Leu Val Leu Ala Ser
 85 90 95
 Leu Phe Phe Arg Pro Val Gly Phe Asp Tyr Arg Ser Lys Ile Glu Glu
 100 105 110
 Thr Arg Trp Arg Asn Met Trp Asp Trp Gly Ile Phe Ile Gly Ser Phe
 115 120 125
 Val Pro Pro Leu Val Ile Gly Val Ala Phe Gly Asn Leu Leu Gln Gly
 130 135 140
 Val Pro Phe Asn Val Asp Glu Tyr Leu Arg Leu Tyr Tyr Thr Gly Asn
 145 150 155 160
 Phe Phe Gln Leu Leu Asn Pro Phe Gly Leu Leu Ala Gly Val Val Ser

165 170 175
 Val Gly Met Ile Ile Thr Gln Gly Ala Thr Tyr Leu Gln Met Arg Thr
 180 185 190
 Val Gly Glu Leu His Leu Arg Thr Arg Ala Thr Ala Gln Val Ala Ala
 195 200 205
 Leu Val Thr Leu Val Cys Phe Ala Leu Ala Gly Val Trp Val Met Tyr
 210 215 220
 Gly Ile Asp Gly Tyr Val Val Lys Ser Thr Met Asp His Tyr Ala Ala
 225 230 235 240
 Ser Asn Pro Leu Asn Lys Glu Val Val Arg Glu Ala Gly Ala Trp Leu
 245 250 255
 Val Asn Phe Asn Asn Thr Pro Ile Leu Trp Ala Ile Pro Ala Leu Gly
 260 265 270
 Val Val Leu Pro Leu Leu Thr Ile Leu Thr Ala Arg Met Asp Lys Ala
 275 280 285
 Ala Trp Ala Phe Val Phe Ser Ser Leu Thr Leu Ala Cys Ile Ile Leu
 290 295 300
 Thr Ala Gly Ile Ala Met Phe Pro Phe Val Met Pro Ser Ser Thr Met
 305 310 315 320
 Met Asn Ala Ser Leu Thr Met Trp Asp Ala Thr Ser Ser Gln Leu Thr
 325 330 335
 Leu Asn Val Met Thr Trp Val Ala Val Val Leu Val Pro Ile Ile Leu
 340 345 350
 Leu Tyr Thr Ala Trp Cys Tyr Trp Lys Met Phe Gly Arg Ile Thr Lys
 355 360 365
 Glu Asp Ile Glu Arg Asn Thr His Ser Leu Tyr
 370 375

<210> 356
 <211> 456
 <212> PRT
 <213> E. Coli

<400> 356
 Met Glu Leu Ser Ser Leu Thr Ala Val Ser Pro Val Asp Gly Arg Tyr
 1 5 10 15
 Gly Asp Lys Val Ser Ala Leu Arg Gly Ile Phe Ser Glu Tyr Gly Leu
 20 25 30
 Leu Lys Phe Arg Val Gln Val Glu Val Arg Trp Leu Gln Lys Leu Ala
 35 40 45
 Ala His Ala Ala Ile Lys Glu Val Pro Ala Phe Ala Ala Asp Ala Ile
 50 55 60
 Gly Tyr Leu Asp Ala Ile Val Ala Ser Phe Ser Glu Glu Asp Ala Ala
 65 70 75 80
 Arg Ile Lys Thr Ile Glu Arg Thr Thr Asn His Asp Val Lys Ala Val
 85 90 95
 Glu Tyr Phe Leu Lys Glu Lys Val Ala Glu Ile Pro Glu Leu His Ala
 100 105 110
 Val Ser Glu Phe Ile His Phe Ala Cys Thr Ser Glu Asp Ile Asn Asn
 115 120 125
 Leu Ser His Ala Leu Met Leu Lys Thr Ala Arg Asp Glu Val Ile Leu
 130 135 140
 Pro Tyr Trp Arg Gln Leu Ile Asp Gly Ile Lys Asp Leu Ala Val Gln
 145 150 155 160
 Tyr Arg Asp Ile Pro Leu Leu Ser Arg Thr His Gly Gln Pro Ala Thr
 165 170 175

Pro Ser Thr Ile Gly Lys Glu Met Ala Asn Val Ala Tyr Arg Met Glu
180 185 190
Arg Gln Tyr Arg Gln Leu Asn Gln Val Glu Ile Leu Gly Lys Ile Asn
195 200 205
Gly Ala Val Gly Asn Tyr Asn Ala His Ile Ala Ala Tyr Pro Glu Val
210 215 220
Asp Trp His Gln Phe Ser Glu Glu Phe Val Thr Ser Leu Gly Ile Gln
225 230 235 240
Trp Asn Pro Tyr Thr Thr Gln Ile Glu Pro His Asp Tyr Ile Ala Glu
245 250 255
Leu Phe Asp Cys Val Ala Arg Phe Asn Thr Ile Leu Ile Asp Phe Asp
260 265 270
Arg Asp Val Trp Gly Tyr Ile Ala Leu Asn His Phe Lys Gln Lys Thr
275 280 285
Ile Ala Gly Glu Ile Gly Ser Ser Thr Met Pro His Lys Val Asn Pro
290 295 300
Ile Asp Phe Glu Asn Ser Glu Gly Asn Leu Gly Leu Ser Asn Ala Val
305 310 315 320
Leu Gln His Leu Ala Ser Lys Leu Pro Val Ser Arg Trp Gln Arg Asp
325 330 335
Leu Thr Asp Ser Thr Val Leu Arg Asn Leu Gly Val Gly Ile Gly Tyr
340 345 350
Ala Leu Ile Ala Tyr Gln Ser Thr Leu Lys Gly Val Ser Lys Leu Glu
355 360 365
Val Asn Arg Asp His Leu Leu Asp Glu Leu Asp His Asn Trp Glu Val
370 375 380
Leu Ala Glu Pro Ile Gln Thr Val Met Arg Arg Tyr Gly Ile Glu Lys
385 390 395 400
Pro Tyr Glu Lys Leu Lys Glu Leu Thr Arg Gly Lys Arg Val Asp Ala
405 410 415
Glu Gly Met Lys Gln Phe Ile Asp Gly Leu Ala Leu Pro Glu Glu Glu
420 425 430
Lys Ala Arg Leu Lys Ala Met Thr Pro Ala Asn Tyr Ile Gly Arg Ala
435 440 445
Ile Thr Met Val Asp Glu Leu Lys
450 455

<210> 357
<211> 61
<212> PRT
<213> E. Coli

<400> 357
Met Leu Ile Leu Thr Arg Arg Val Gly Glu Thr Leu Met Ile Gly Asp
1 5 10 15
Glu Val Thr Val Thr Val Leu Gly Val Lys Gly Asn Gln Val Arg Ile
20 25 30
Gly Val Asn Ala Pro Lys Glu Val Ser Val His Arg Glu Glu Ile Tyr
35 40 45
Gln Arg Ile Gln Ala Glu Lys Ser Gln Gln Ser Ser Tyr
50 55 60

<210> 358
<211> 83
<212> RNA

<213> E. Coli

<400> 358

ggugaggugg ccgagaggcu gaaggcgcuc ccugcuaag ggaguaugcg gucaaaagcu 60
gcauccgggg uucgaaucce cgccucaccg cca 83

<210> 359

<211> 200

<212> PRT

<213> E. Coli

<400> 359

Meu Lys Asn Lys Ala Asp Asn Lys Lys Arg Asn Phe Leu Thr His Ser
1 5 10 15
Glu Ile Glu Ser Leu Leu Lys Ala Ala Asn Thr Gly Pro His Ala Ala
20 25 30
Arg Asn Tyr Cys Leu Thr Leu Leu Cys Phe Ile His Gly Phe Arg Ala
35 40 45
Ser Glu Ile Cys Arg Leu Arg Ile Ser Asp Ile Asp Leu Lys Ala Lys
50 55 60
Cys Ile Tyr Ile His Arg Leu Lys Lys Gly Phe Ser Thr Thr His Pro
65 70 75 80
Leu Leu Asn Lys Glu Val Gln Ala Leu Lys Asn Trp Leu Ser Ile Arg
85 90 95
Thr Ser Tyr Pro His Ala Glu Ser Glu Trp Val Phe Leu Ser Arg Lys
100 105 110
Gly Asn Pro Leu Ser Arg Gln Gln Phe Tyr His Ile Ile Ser Thr Ser
115 120 125
Gly Gly Asn Ala Gly Leu Ser Leu Glu Ile His Pro His Met Leu Arg
130 135 140
His Ser Cys Gly Phe Ala Leu Ala Asn Met Gly Ile Asp Thr Arg Leu
145 150 155 160
Ile Gln Asp Tyr Leu Gly His Arg Asn Ile Arg His Thr Val Trp Tyr
165 170 175
Thr Ala Ser Asn Ala Gly Arg Phe Tyr Gly Ile Trp Asp Arg Ala Arg
180 185 190
Gly Arg Gln Arg His Ala Val Leu
195 200

<210> 360

<211> 198

<212> PRT

<213> E. Coli

<400> 360

Met Ser Lys Arg Tyr Leu Thr Gly Lys Glu Val Gln Ala Met Met
1 5 10 15
Gln Ala Val Cys Tyr Gly Ala Thr Gly Ala Arg Asp Tyr Cys Leu Ile
20 25 30
Leu Leu Ala Tyr Arg His Gly Met Arg Ile Ser Glu Leu Leu Asp Leu
35 40 45
His Tyr Gln Asp Leu Asp Leu Asn Glu Gly Arg Ile Asn Ile Arg Arg
50 55 60
Leu Lys Asn Gly Phe Ser Thr Val His Pro Leu Arg Phe Asp Glu Arg
65 70 75 80

Glu Ala Val Glu Arg Trp Thr Gln Glu Arg Ala Asn Trp Lys Gly Ala
85 90 95
Asp Arg Thr Asp Ala Ile Phe Ile Ser Arg Arg Gly Ser Arg Leu Ser
100 105 110
Arg Gln Gln Ala Tyr Arg Ile Ile Arg Asp Ala Gly Ile Glu Ala Gly
115 120 125
Thr Val Thr Gln Thr His Pro His Met Leu Arg His Ala Cys Gly Tyr
130 135 140
Glu Leu Ala Glu Arg Gly Ala Asp Thr Arg Leu Ile Gln Asp Tyr Leu
145 150 155 160
Gly His Arg Asn Ile Arg His Thr Val Arg Tyr Thr Ala Ser Asn Ala
165 170 175
Ala Arg Phe Ala Gly Leu Trp Glu Arg Asn Asn Leu Ile Asn Glu Lys
180 185 190
Leu Lys Arg Glu Glu Val
195

<210> 361
<211> 182
<212> PRT
<213> E. Coli

<400> 361
Met Lys Ile Lys Thr Leu Ala Ile Val Val Leu Ser Ala Leu Ser Leu
1 5 10 15
Ser Ser Thr Ala Ala Leu Ala Ala Thr Thr Val Asn Gly Gly Thr
20 25 30
Val His Phe Lys Gly Glu Val Val Asn Ala Ala Cys Ala Val Asp Ala
35 40 45
Gly Ser Val Asp Gln Thr Val Gln Leu Gly Gln Val Arg Thr Ala Ser
50 55 60
Leu Ala Gln Glu Gly Ala Thr Ser Ser Ala Val Gly Phe Asn Ile Gln
65 70 75 80
Leu Asn Asp Cys Asp Thr Asn Val Ala Ser Lys Ala Ala Val Ala Phe
85 90 95
Leu Gly Thr Ala Ile Asp Ala Gly His Thr Asn Val Leu Ala Leu Gln
100 105 110
Ser Ser Ala Ala Gly Ser Ala Thr Asn Val Gly Val Gln Ile Leu Asp
115 120 125
Arg Thr Gly Ala Ala Leu Thr Leu Asp Gly Ala Thr Phe Ser Ser Glu
130 135 140
Thr Thr Leu Asn Asn Gly Thr Asn Thr Ile Pro Phe Gln Ala Arg Tyr
145 150 155 160
Phe Ala Thr Gly Ala Ala Thr Pro Gly Ala Ala Asn Ala Asp Ala Thr
165 170 175
Phe Lys Val Gln Tyr Gln
180

<210> 362
<211> 215
<212> PRT
<213> E. Coli

<400> 362

Met	Leu	Leu	Met	Arg	Met	Arg	Pro	Ser	Arg	Phe	Ser	Ile	Asn	Asn	Leu
1				5					10					15	
Pro	Arg	Phe	Arg	Asp	Val	Ile	Thr	Gly	Arg	Asp	Ala	His	Pro	Cys	Ala
		20						25					30		
Ile	Lys	Ile	Thr	Met	Lys	Arg	Lys	Arg	Leu	Phe	Leu	Leu	Ala	Ser	Leu
	35						40					45			
Leu	Pro	Met	Phe	Ala	Leu	Ala	Gly	Asn	Lys	Trp	Asn	Thr	Thr	Leu	Pro
	50					55					60				
Gly	Gly	Asn	Met	Gln	Phe	Gln	Gly	Val	Ile	Ile	Ala	Glu	Thr	Cys	Arg
65				70						75					80
Ile	Glu	Ala	Gly	Asp	Lys	Gln	Met	Thr	Val	Asn	Met	Gly	Gln	Ile	Ser
				85					90					95	
Ser	Asn	Arg	Phe	His	Ala	Val	Gly	Glu	Asp	Ser	Ala	Pro	Val	Pro	Phe
			100					105					110		
Val	Ile	His	Leu	Arg	Glu	Cys	Ser	Thr	Val	Val	Ser	Glu	Arg	Val	Gly
		115					120					125			
Val	Ala	Phe	His	Gly	Val	Ala	Asp	Gly	Lys	Asn	Pro	Asp	Val	Leu	Ser
	130					135					140				
Val	Gly	Glu	Gly	Pro	Gly	Ile	Ala	Thr	Asn	Ile	Gly	Val	Ala	Leu	Phe
145					150					155					160
Asp	Asp	Glu	Gly	Asn	Leu	Val	Pro	Ile	Asn	Arg	Pro	Pro	Ala	Asn	Trp
				165					170					175	
Lys	Arg	Leu	Tyr	Ser	Gly	Ser	Thr	Ser	Leu	His	Phe	Ile	Ala	Lys	Tyr
			180					185					190		
Arg	Ala	Thr	Gly	Arg	Arg	Val	Thr	Gly	Gly	Ile	Ala	Asn	Ala	Gln	Ala
		195					200					205			
Trp	Phe	Ser	Leu	Thr	Tyr	Gln									
	210					215									

<210> 363

<211> 241

<212> PRT

<213> E. Coli

<400> 363

Met	Ser	Asn	Lys	Asn	Val	Asn	Val	Arg	Lys	Ser	Gln	Glu	Ile	Thr	Phe
1				5					10					15	
Cys	Leu	Leu	Ala	Gly	Ile	Leu	Met	Phe	Met	Ala	Met	Met	Val	Ala	Gly
		20						25					30		
Arg	Ala	Glu	Ala	Gly	Val	Ala	Leu	Gly	Ala	Thr	Arg	Val	Ile	Tyr	Pro
		35					40					45			
Ala	Gly	Gln	Lys	Gln	Glu	Gln	Leu	Ala	Val	Thr	Asn	Asn	Asp	Glu	Asn
	50					55					60				
Ser	Thr	Tyr	Leu	Ile	Gln	Ser	Trp	Val	Glu	Asn	Ala	Asp	Gly	Val	Lys
65				70						75					80
Asp	Gly	Arg	Phe	Ile	Val	Thr	Pro	Pro	Leu	Phe	Ala	Met	Lys	Gly	Lys
			85					90					95		
Lys	Glu	Asn	Thr	Leu	Arg	Ile	Leu	Asp	Ala	Thr	Asn	Asn	Gln	Leu	Pro
			100					105					110		
Gln	Asp	Arg	Glu	Ser	Leu	Phe	Trp	Met	Asn	Val	Lys	Ala	Ile	Pro	Ser
		115					120					125			
Met	Asp	Lys	Ser	Lys	Leu	Thr	Glu	Asn	Thr	Leu	Gln	Leu	Ala	Ile	Ile
	130					135					140				
Ser	Arg	Ile	Lys	Leu	Tyr	Tyr	Arg	Pro	Ala	Lys	Leu	Ala	Leu	Pro	Pro
145					150					155					160

Asp Gln Ala Ala Glu Lys Leu Arg Phe Arg Arg Ser Ala Asn Ser Leu
 165 170 175
 Thr Leu Ile Asn Pro Thr Pro Tyr Tyr Leu Thr Val Thr Glu Leu Asn
 180 185 190
 Ala Gly Thr Arg Val Leu Glu Asn Ala Leu Val Pro Pro Met Gly Glu
 195 200 205
 Ser Thr Val Lys Leu Pro Ser Asp Ala Gly Ser Asn Ile Thr Tyr Arg
 210 215 220
 Thr Ile Asn Asp Tyr Gly Ala Leu Thr Pro Lys Met Thr Gly Val Met
 225 230 235 240
 Glu

<210> 364
 <211> 878
 <212> PRT
 <213> E. Coli

<400> 364
 Met Ser Tyr Leu Asn Leu Arg Leu Tyr Gln Arg Asn Thr Gln Cys Leu
 1 5 10 15
 His Ile Arg Lys His Arg Leu Ala Gly Phe Phe Val Arg Leu Val Val
 20 25 30
 Ala Cys Ala Phe Ala Ala Gln Ala Pro Leu Ser Ser Ala Asp Leu Tyr
 35 40 45
 Phe Asn Pro Arg Phe Leu Ala Asp Asp Pro Gln Ala Val Ala Asp Leu
 50 55 60
 Ser Arg Phe Glu Asn Gly Gln Glu Leu Pro Pro Gly Thr Tyr Arg Val
 65 70 75 80
 Asp Ile Tyr Leu Asn Asn Gly Tyr Met Ala Thr Arg Asp Val Thr Phe
 85 90 95
 Asn Thr Gly Asp Ser Glu Gln Gly Ile Val Pro Cys Leu Thr Arg Ala
 100 105 110
 Gln Leu Ala Ser Met Gly Leu Asn Thr Ala Ser Val Ala Gly Met Asn
 115 120 125
 Leu Leu Ala Asp Asp Ala Cys Val Pro Leu Thr Thr Met Val Gln Asp
 130 135 140
 Ala Thr Ala His Leu Asp Val Gly Gln Gln Arg Leu Asn Leu Thr Ile
 145 150 155 160
 Pro Gln Ala Phe Met Ser Asn Arg Ala Arg Gly Tyr Ile Pro Pro Glu
 165 170 175
 Leu Trp Asp Pro Gly Ile Asn Ala Gly Leu Leu Asn Tyr Asn Phe Ser
 180 185 190
 Gly Asn Ser Val Gln Asn Arg Ile Gly Gly Asn Ser His Tyr Ala Tyr
 195 200 205
 Leu Asn Leu Gln Ser Gly Leu Asn Ile Gly Ala Trp Arg Leu Arg Asp
 210 215 220
 Asn Thr Thr Trp Ser Tyr Asn Ser Ser Asp Arg Ser Ser Gly Ser Lys
 225 230 235 240
 Asn Lys Trp Gln His Ile Asn Thr Trp Leu Glu Arg Asp Ile Ile Pro
 245 250 255
 Leu Arg Ser Arg Leu Thr Leu Gly Asp Gly Tyr Thr Gln Gly Asp Ile
 260 265 270
 Phe Asp Gly Ile Asn Phe Arg Gly Ala Gln Leu Ala Ser Asp Asp Asn
 275 280 285
 Met Leu Pro Asp Ser Gln Arg Gly Phe Ala Pro Val Ile His Gly Ile

290	295	300
Ala Arg Gly Thr Ala Gln Val Thr Ile Lys Gln Asn Gly Tyr Asp Ile		
305	310	315
Tyr Asn Ser Thr Val Pro Pro Gly Pro Phe Thr Ile Asn Asp Ile Tyr		320
	325	330
Ala Ala Gly Asn Ser Gly Asp Leu Gln Val Thr Ile Lys Glu Ala Asp		335
	340	345
Gly Ser Thr Gln Ile Phe Thr Val Pro Tyr Ser Ser Val Pro Leu Leu		350
	355	360
Gln Arg Glu Gly His Thr Arg Tyr Ser Ile Thr Ala Gly Glu Tyr Arg		365
	370	375
Ser Gly Asn Ala Gln Gln Lys Thr Arg Phe Phe Gln Ser Thr Leu		380
385	390	395
Leu His Gly Leu Pro Ala Gly Trp Thr Ile Tyr Gly Gly Thr Gln Leu		400
	405	410
Ala Asp Arg Tyr Arg Ala Phe Asn Phe Gly Ile Gly Lys Asn Met Gly		415
	420	425
Ala Leu Gly Ala Leu Ser Val Asp Met Thr Gln Ala Asn Ser Thr Leu		430
	435	440
Pro Asp Asp Ser Gln His Asp Gly Gln Ser Val Arg Phe Leu Tyr Asn		445
	450	455
Lys Ser Leu Asn Glu Ser Gly Thr Asn Ile Gln Leu Val Gly Tyr Arg		460
465	470	475
Tyr Ser Thr Ser Gly Tyr Phe Asn Phe Ala Asp Thr Thr Tyr Ser Arg		480
	485	490
Met Asn Gly Tyr Asn Ile Glu Thr Gln Asp Gly Val Ile Gln Val Lys		495
	500	505
Pro Lys Phe Thr Asp Tyr Tyr Asn Leu Ala Tyr Asn Lys Arg Gly Lys		510
	515	520
Leu Gln Leu Thr Val Thr Gln Gln Leu Gly Arg Thr Ser Thr Leu Tyr		525
	530	535
Leu Ser Gly Ser His Gln Thr Tyr Trp Gly Thr Ser Asn Val Asp Glu		540
545	550	555
Gln Phe Gln Ala Gly Leu Asn Thr Ala Phe Glu Asp Ile Asn Trp Thr		560
	565	570
Leu Ser Tyr Ser Leu Thr Lys Asn Ala Trp Gln Lys Gly Arg Asp Gln		575
	580	585
Met Leu Ala Leu Asn Val Asn Ile Pro Phe Ser His Trp Leu Arg Ser		590
	595	600
Asp Ser Lys Ser Gln Trp Arg His Ala Ser Ala Ser Tyr Ser Met Ser		605
	610	615
His Asp Leu Asn Gly Arg Met Thr Asn Leu Ala Gly Val Tyr Gly Thr		620
625	630	635
Leu Leu Glu Asp Asn Asn Leu Ser Tyr Ser Val Gln Thr Gly Tyr Ala		640
	645	650
Gly Gly Gly Asp Gly Asn Ser Gly Ser Thr Gly Tyr Ala Thr Leu Asn		655
	660	665
Tyr Arg Gly Gly Tyr Gly Asn Ala Asn Ile Gly Tyr Ser His Ser Asp		670
	675	680
Asp Ile Lys Gln Leu Tyr Tyr Gly Val Ser Gly Gly Val Leu Ala His		685
	690	695
Ala Asn Gly Val Thr Leu Gly Gln Pro Leu Asn Asp Thr Val Val Leu		700
705	710	715
Val Lys Ala Pro Gly Ala Lys Asp Ala Lys Val Glu Asn Gln Thr Gly		720
	725	730
Val Arg Thr Asp Trp Arg Gly Tyr Ala Val Leu Pro Tyr Ala Thr Glu		735
	740	745
		750

Tyr Arg Glu Asn Arg Val Ala Leu Asp Thr Asn Thr Leu Ala Asp Asn
755 760 765
Val Asp Leu Asp Asn Ala Val Ala Asn Val Val Pro Thr Arg Gly Ala
770 775 780
Ile Val Arg Ala Glu Phe Lys Ala Arg Val Gly Ile Lys Leu Leu Met
785 790 795 800
Thr Leu Thr His Asn Asn Lys Pro Leu Pro Phe Gly Ala Met Val Thr
805 810 815
Ser Glu Ser Ser Gln Ser Ser Gly Ile Val Ala Asp Asn Gly Gln Val
820 825 830
Tyr Leu Ser Gly Met Pro Leu Ala Gly Lys Val Gln Val Lys Trp Gly
835 840 845
Glu Glu Glu Asn Ala His Cys Val Ala Asn Tyr Gln Leu Pro Pro Glu
850 855 860
Ser Gln Gln Gln Leu Leu Thr Gln Leu Ser Ala Glu Cys Arg
865 870 875

<210> 365
<211> 176
<212> PRT
<213> E. Coli

<400> 365
Met Arg Asn Lys Pro Phe Tyr Leu Leu Cys Ala Phe Leu Trp Leu Ala
1 5 10 15
Val Ser His Ala Leu Ala Ala Asp Ser Thr Ile Thr Ile Arg Gly Tyr
20 25 30
Val Arg Asp Asn Gly Cys Ser Val Ala Ala Glu Ser Thr Asn Phe Thr
35 40 45
Val Asp Leu Met Glu Asn Ala Lys Gln Phe Asn Asn Ile Gly Ala
50 55 60
Thr Thr Pro Val Val Pro Phe Arg Ile Leu Leu Ser Pro Cys Gly Asn
65 70 75 80
Ala Val Ser Ala Val Lys Val Gly Phe Thr Gly Val Ala Asp Ser His
85 90 95
Asn Ala Asn Leu Leu Ala Leu Glu Asn Thr Val Ser Ala Ala Ser Gly
100 105 110
Leu Gly Ile Gln Leu Leu Asn Glu Gln Gln Asn Gln Ile Pro Leu Asn
115 120 125
Ala Pro Ser Ser Ala Leu Ser Trp Thr Thr Leu Thr Pro Gly Lys Pro
130 135 140
Asn Thr Leu Asn Phe Tyr Ala Arg Leu Met Ala Thr Gln Val Pro Val
145 150 155 160
Thr Ala Gly His Ile Asn Ala Thr Ala Thr Phe Thr Leu Glu Tyr Gln
165 170 175

<210> 366
<211> 167
<212> PRT
<213> E. Coli

<400> 366
Met Lys Trp Cys Lys Arg Gly Tyr Val Leu Ala Ala Ile Leu Ala Leu
1 5 10 15

Ala	Ser	Ala	Thr	Ile	Gln	Ala	Ala	Asp	Val	Thr	Ile	Thr	Val	Asn	Gly
			20					25					30		
Lys	Val	Val	Ala	Lys	Pro	Cys	Thr	Val	Ser	Thr	Thr	Asn	Ala	Thr	Val
		35					40					45			
Asp	Leu	Gly	Asp	Leu	Tyr	Ser	Phe	Ser	Leu	Met	Ser	Ala	Gly	Ala	Ala
	50					55					60				
Ser	Ala	Trp	His	Asp	Val	Ala	Leu	Glu	Leu	Thr	Asn	Cys	Pro	Val	Gly
65					70					75					80
Thr	Ser	Arg	Val	Thr	Ala	Ser	Phe	Ser	Gly	Ala	Ala	Asp	Ser	Thr	Gly
			85						90					95	
Tyr	Tyr	Lys	Asn	Gln	Gly	Thr	Ala	Gln	Asn	Ile	Gln	Leu	Glu	Leu	Gln
			100					105					110		
Asp	Asp	Ser	Gly	Asn	Thr	Leu	Asn	Thr	Gly	Ala	Thr	Lys	Thr	Val	Gln
		115					120					125			
Val	Asp	Asp	Ser	Ser	Gln	Ser	Ala	His	Phe	Pro	Leu	Gln	Val	Arg	Ala
	130					135					140				
Leu	Thr	Val	Asn	Gly	Gly	Ala	Thr	Gln	Gly	Thr	Ile	Gln	Ala	Val	Ile
145					150					155					160
Ser	Ile	Thr	Tyr	Thr	Tyr	Ser									
				165											

<210> 367
 <211> 300
 <212> PRT
 <213> E. Coli

Met	Lys	Arg	Val	Ile	Thr	Leu	Phe	Ala	Val	Leu	Leu	Met	Gly	Trp	Ser
1				5					10					15	
Val	Asn	Ala	Trp	Ser	Phe	Ala	Cys	Lys	Thr	Ala	Asn	Gly	Thr	Ala	Ile
			20					25					30		
Pro	Ile	Gly	Gly	Gly	Ser	Ala	Asn	Val	Tyr	Val	Asn	Leu	Ala	Pro	Val
		35					40					45			
Val	Asn	Val	Gly	Gln	Asn	Leu	Val	Val	Asp	Leu	Ser	Thr	Gln	Ile	Phe
	50					55					60				
Cys	His	Asn	Asp	Tyr	Pro	Glu	Thr	Ile	Thr	Asp	Tyr	Val	Thr	Leu	Gln
65					70					75					80
Arg	Gly	Ser	Ala	Tyr	Gly	Gly	Val	Leu	Ser	Asn	Phe	Ser	Gly	Thr	Val
				85					90					95	
Lys	Tyr	Ser	Gly	Ser	Ser	Tyr	Pro	Phe	Pro	Thr	Thr	Ser	Glu	Thr	Pro
			100					105					110		
Arg	Val	Val	Tyr	Asn	Ser	Arg	Thr	Asp	Lys	Pro	Trp	Pro	Val	Ala	Leu
		115					120					125			
Tyr	Leu	Thr	Pro	Val	Ser	Ser	Ala	Gly	Gly	Val	Ala	Ile	Lys	Ala	Gly
	130					135					140				
Ser	Leu	Ile	Ala	Val	Leu	Ile	Leu	Arg	Gln	Thr	Asn	Asn	Tyr	Asn	Ser
145					150					155					160
Asp	Asp	Phe	Gln	Phe	Val	Trp	Asn	Ile	Tyr	Ala	Asn	Asn	Asp	Val	Val
				165					170					175	
Val	Pro	Thr	Gly	Gly	Cys	Asp	Val	Ser	Ala	Arg	Asp	Val	Thr	Val	Thr
			180					185					190		
Leu	Pro	Asp	Tyr	Pro	Gly	Ser	Val	Pro	Ile	Pro	Leu	Thr	Val	Tyr	Cys
		195					200					205			
Ala	Lys	Ser	Gln	Asn	Leu	Gly	Tyr	Tyr	Leu	Ser	Gly	Thr	Thr	Ala	Asp
	210					215					220				

Ala Gly Asn Ser Ile Phe Thr Asn Thr Ala Ser Phe Ser Pro Ala Gln
 225 230 235 240
 Gly Val Gly Val Gln Leu Thr Arg Asn Gly Thr Ile Ile Pro Ala Asn
 245 250 255
 Asn Thr Val Ser Leu Gly Ala Val Gly Thr Ser Ala Val Ser Leu Gly
 260 265 270
 Leu Thr Ala Asn Tyr Ala Arg Thr Gly Gly Gln Val Thr Ala Gly Asn
 275 280 285
 Val Gln Ser Ile Ile Gly Val Thr Phe Val Tyr Gln
 290 295 300

<210> 368
 <211> 521
 <212> PRT
 <213> E. Coli

<400> 368
 Met Leu Ser Lys Leu Pro Arg Arg Leu Arg Ser Phe Gln Thr Tyr Cys
 1 5 10 15
 Thr Ile Arg Val His Arg Gly Glu Asp Met Lys Ser Met Asp Lys Leu
 20 25 30
 Thr Thr Gly Val Ala Tyr Gly Thr Ser Ala Gly Asn Ala Gly Phe Trp
 35 40 45
 Ala Leu Gln Leu Leu Asp Lys Val Thr Pro Ser Gln Trp Ala Ala Ile
 50 55 60
 Gly Val Leu Gly Ser Leu Val Phe Gly Leu Leu Thr Tyr Leu Thr Asn
 65 70 75 80
 Leu Tyr Phe Lys Ile Lys Glu Asp Arg Arg Lys Ala Ala Arg Gly Glu
 85 90 95
 Ser Asn Asp Ser Arg Leu Thr Gly Cys Glu Arg Ser Pro Phe Glu Ser
 100 105 110
 Tyr Gly Asn Cys Ser Leu Thr Gly Gln Arg Thr Leu Arg Asn Phe Pro
 115 120 125
 Gly Cys Arg His Gly Pro Cys Arg Ser Cys Ala Gly Val Leu Gly Ser
 130 135 140
 Ser Gln Lys Glu Arg Pro Ala Ser Leu Pro Gly Ser Ser Arg Lys Ile
 145 150 155 160
 Val Arg Lys Ser Val Leu Ser Ala Ala Ser Val Leu Leu Asp Lys Ser
 165 170 175
 Cys Gln Ala Arg Ala Ser Ser Ser Ile Ser Met Asn Thr Lys Ile Arg
 180 185 190
 Tyr Gly Leu Ser Ala Ala Val Leu Ala Leu Ile Gly Ala Gly Ala Ser
 195 200 205
 Ala Pro Gln Ile Leu Asp Gln Phe Leu Asp Glu Lys Glu Gly Asn His
 210 215 220
 Thr Met Ala Tyr Arg Asp Gly Ser Gly Ile Trp Thr Ile Cys Arg Gly
 225 230 235 240
 Ala Thr Val Val Asp Gly Lys Thr Val Phe Pro Asn Met Lys Leu Ser
 245 250 255
 Lys Glu Lys Cys Asp Gln Val Asn Ala Ile Glu Arg Asp Lys Ala Leu
 260 265 270
 Ala Trp Val Glu Arg Asn Ile Lys Val Pro Leu Thr Glu Pro Gln Lys
 275 280 285
 Ala Gly Ile Ala Ser Phe Cys Pro Tyr Asn Ile Gly Pro Gly Lys Cys
 290 295 300

Phe Pro Ser Thr Phe Tyr Lys Arg Leu Asn Ala Gly Asp Arg Lys Gly
 305 310 315 320
 Ala Cys Glu Ala Ile Arg Trp Trp Ile Lys Asp Gly Gly Arg Asp Cys
 325 330 335
 Arg Ile Arg Ser Asn Asn Cys Tyr Gly Gln Val Ile Arg Arg Asp Gln
 340 345 350
 Glu Ser Ala Leu Thr Cys Trp Gly Ile Glu Gln Ile Arg Tyr Ser Trp
 355 360 365
 Phe Phe Ser Cys Cys Gln Asp Leu Ser Ser Glu Met Ser Gly Ala Thr
 370 375 380
 Glu Asp Gly Lys Lys Asn Gly Arg Asn Val Met Leu Pro His Tyr His
 385 390 395 400
 Lys Arg Met Leu Asn Leu Leu Glu Leu Asn Arg Gly Glu Leu Pro
 405 410 415
 Val Met Arg Leu Leu Lys Met Arg Asn Arg Asn Leu Leu Lys Phe Leu
 420 425 430
 Pro Gly Leu Leu Ile Cys Leu Ile Val Leu Thr Ser Cys Val Pro Lys
 435 440 445
 Gln Lys Asn Met Pro Tyr Ala Leu Thr Gln Arg Ser Ile Pro Gln Ile
 450 455 460
 Leu Pro Leu Pro Ser Glu Ala Lys Gln Pro Lys Pro Pro Lys Glu Cys
 465 470 475 480
 Ser Pro Thr Cys Ser Glu Ile Leu Gln Gln Lys Leu Ser Phe Met Leu
 485 490 495
 Lys Leu Leu Thr Asn Ala Thr Ser Gln Glu Leu Val Asn Arg Ser Met
 500 505 510
 Asn Leu Glu Ile Lys Ser Ile Lys Cys
 515 520

<210> 369
 <211> 177
 <212> PRT
 <213> E. Coli

<400> 369

Met Asn Thr Lys Ile Arg Tyr Gly Leu Ser Ala Ala Val Leu Ala Leu
 1 5 10 15
 Ile Gly Ala Gly Ala Ser Ala Pro Gln Ile Leu Asp Gln Phe Leu Asp
 20 25 30
 Glu Lys Glu Gly Asn His Thr Met Ala Tyr Arg Asp Gly Ser Gly Ile
 35 40 45
 Trp Thr Ile Cys Arg Gly Ala Thr Val Val Asp Gly Lys Thr Val Phe
 50 55 60
 Pro Asn Met Lys Leu Ser Lys Glu Lys Cys Asp Gln Val Asn Ala Ile
 65 70 75 80
 Glu Arg Asp Lys Ala Leu Ala Trp Val Glu Arg Asn Ile Lys Val Pro
 85 90 95
 Leu Thr Glu Pro Gln Lys Ala Gly Ile Ala Ser Phe Cys Pro Tyr Asn
 100 105 110
 Ile Gly Pro Gly Lys Cys Phe Pro Ser Thr Phe Tyr Lys Arg Leu Asn
 115 120 125
 Ala Gly Asp Arg Lys Gly Ala Cys Glu Ala Ile Arg Trp Trp Ile Lys
 130 135 140
 Asp Gly Gly Arg Asp Cys Arg Ile Arg Ser Asn Asn Cys Tyr Gly Gln
 145 150 155 160

Val Ile Arg Arg Asp Gln Glu Ser Ala Leu Thr Cys Trp Gly Ile Glu
 165 170 175
 Gln

<210> 370
 <211> 103
 <212> PRT
 <213> E. Coli

<400> 370
 Met Thr Gln Asp Tyr Glu Leu Val Val Lys Gly Val Arg Asn Phe Glu
 1 5 10 15
 Asn Lys Val Thr Val Thr Val Ala Leu Gln Asp Lys Glu Arg Phe Asp
 20 25 30
 Gly Glu Ile Phe Asp Leu Asp Val Ala Met Asp Arg Val Glu Gly Ala
 35 40 45
 Ala Leu Glu Phe Tyr Glu Ala Ala Ala Arg Arg Ser Val Arg Gln Val
 50 55 60
 Phe Leu Glu Val Ala Glu Lys Leu Ser Glu Lys Val Glu Ser Tyr Leu
 65 70 75 80
 Gln His Gln Tyr Ser Phe Lys Ile Glu Asn Pro Ala Asn Lys His Glu
 85 90 95
 Arg Pro His His Lys Tyr Leu
 100

<210> 371
 <211> 96
 <212> PRT
 <213> E. Coli

<400> 371
 Met Leu Ser Lys Leu Pro Arg Arg Leu Arg Ser Phe Gln Thr Tyr Cys
 1 5 10 15
 Thr Ile Arg Val His Arg Gly Glu Asp Met Lys Ser Met Asp Lys Leu
 20 25 30
 Thr Thr Gly Val Ala Tyr Gly Thr Ser Ala Gly Asn Ala Gly Phe Trp
 35 40 45
 Ala Leu Gln Leu Leu Asp Lys Val Thr Pro Ser Gln Trp Ala Ala Ile
 50 55 60
 Gly Val Leu Gly Ser Leu Val Phe Gly Leu Leu Thr Tyr Leu Thr Asn
 65 70 75 80
 Leu Tyr Phe Lys Ile Lys Glu Asp Arg Arg Lys Ala Ala Arg Gly Glu
 85 90 95

<210> 372
 <211> 71
 <212> PRT
 <213> E. Coli

<400> 372
 Met Ser Asn Lys Met Thr Gly Leu Val Lys Trp Phe Asn Ala Asp Lys

1				5					10				15		
Gly	Phe	Gly	Phe	Ile	Ser	Pro	Val	Asp	Gly	Ser	Lys	Asp	Val	Phe	Val
			20					25					30		
His	Phe	Ser	Ala	Ile	Gln	Asn	Asp	Asn	Tyr	Arg	Thr	Leu	Phe	Glu	Gly
		35					40					45			
Gln	Lys	Val	Thr	Phe	Ser	Ile	Glu	Ser	Gly	Ala	Lys	Gly	Pro	Ala	Ala
	50					55					60				
Ala	Asn	Val	Ile	Ile	Thr	Asp									
65					70										

<210> 373
 <211> 338
 <212> PRT
 <213> E. Coli

Met	Phe	Val	Ile	Trp	Ser	His	Arg	Thr	Gly	Phe	Ile	Met	Ser	His	Gln
1				5					10					15	
Leu	Thr	Phe	Ala	Asp	Ser	Glu	Phe	Ser	Ser	Lys	Arg	Arg	Gln	Thr	Arg
			20					25					30		
Lys	Glu	Ile	Phe	Leu	Ser	Arg	Met	Glu	Gln	Ile	Leu	Pro	Trp	Gln	Asn
		35					40					45			
Met	Val	Glu	Val	Ile	Glu	Pro	Phe	Tyr	Pro	Lys	Ala	Gly	Asn	Gly	Arg
	50				55						60				
Arg	Pro	Tyr	Pro	Leu	Glu	Thr	Met	Leu	Arg	Ile	His	Cys	Met	Gln	His
65				70					75					80	
Trp	Tyr	Asn	Leu	Ser	Asp	Gly	Ala	Met	Glu	Asp	Ala	Leu	Tyr	Glu	Ile
			85						90					95	
Ala	Ser	Met	Arg	Leu	Phe	Ala	Arg	Leu	Ser	Leu	Asp	Ser	Ala	Leu	Pro
			100					105					110		
Asp	Arg	Thr	Thr	Ile	Met	Asn	Phe	Arg	His	Leu	Leu	Glu	Gln	His	Gln
			115				120					125			
Leu	Ala	Arg	Gln	Leu	Phe	Lys	Thr	Ile	Asn	Arg	Trp	Leu	Ala	Glu	Ala
	130					135					140				
Gly	Val	Met	Met	Thr	Gln	Gly	Thr	Leu	Val	Asp	Ala	Thr	Ile	Ile	Glu
145					150					155				160	
Ala	Pro	Ser	Ser	Thr	Lys	Asn	Lys	Glu	Gln	Gln	Arg	Asp	Pro	Glu	Met
				165					170					175	
His	Gln	Thr	Lys	Lys	Gly	Asn	Gln	Trp	His	Phe	Gly	Met	Lys	Ala	His
			180					185					190		
Ile	Gly	Val	Asp	Ala	Lys	Ser	Gly	Leu	Thr	His	Ser	Leu	Val	Thr	Thr
	195						200					205			
Ala	Ala	Asn	Glu	His	Asp	Leu	Asn	Gln	Leu	Gly	Asn	Leu	Leu	His	Gly
	210					215					220				
Glu	Glu	Gln	Phe	Val	Ser	Ala	Asp	Ala	Gly	Tyr	Gln	Gly	Ala	Pro	Gln
225					230					235				240	
Arg	Glu	Glu	Leu	Ala	Glu	Val	Asp	Val	Asp	Trp	Leu	Ile	Ala	Glu	Arg
			245						250					255	
Pro	Gly	Lys	Val	Arg	Thr	Leu	Lys	Gln	His	Pro	Arg	Lys	Asn	Lys	Thr
			260					265					270		
Ala	Ile	Asn	Ile	Glu	Tyr	Met	Lys	Ala	Ser	Ile	Arg	Ala	Arg	Val	Glu
	275						280					285			
His	Pro	Phe	Arg	Ile	Ile	Lys	Arg	Gln	Phe	Gly	Phe	Val	Lys	Ala	Arg
	290					295					300				
Tyr	Lys	Gly	Leu	Leu	Lys	Asn	Asp	Asn	Gln	Leu	Ala	Met	Leu	Phe	Thr

[illegible]

<210>	376
<211>	196
<212>	PRT
<213>	E. Coli

<400> 376															
Met	Ile	Leu	Lys	Leu	Ala	Lys	Arg	Tyr	Gly	Leu	Cys	Gly	Phe	Ile	Arg
1				5					10					15	
Leu	Val	Arg	Asp	Val	Leu	Leu	Thr	Arg	Val	Phe	Tyr	Arg	Asn	Cys	Arg
			20					25					30		
Ile	Ile	Arg	Phe	Pro	Cys	Tyr	Ile	Arg	Asn	Asp	Gly	Ser	Ile	Asn	Phe
			35				40					45			
Gly	Glu	Asn	Phe	Thr	Ser	Gly	Val	Gly	Leu	Arg	Leu	Asp	Ala	Phe	Gly
	50					55					60				
Arg	Gly	Val	Ile	Phe	Phe	Ser	Asp	Asn	Val	Gln	Val	Asn	Asp	Tyr	Val
65					70					75				80	
His	Ile	Ala	Ser	Ile	Glu	Ser	Val	Thr	Ile	Gly	Arg	Asp	Thr	Leu	Ile
				85					90					95	
Ala	Ser	Lys	Val	Phe	Ile	Thr	Asp	His	Asn	His	Gly	Ser	Phe	Lys	His
			100					105					110		
Ser	Asp	Pro	Met	Ser	Ser	Pro	Asn	Ile	Pro	Pro	Asp	Met	Arg	Thr	Leu
			115				120					125			

Glu Ser Ser Ala Val Val Ile Gly Gln Arg Val Trp Leu Gly Glu Asn
 130 135 140
 Val Thr Val Leu Pro Gly Thr Ile Ile Gly Asn Gly Val Val Val Gly
 145 150 155 160
 Ala Asn Ser Val Val Arg Gly Ser Ile Pro Glu Asn Thr Val Ile Ala
 165 170 175
 Gly Val Pro Ala Lys Ile Ile Lys Lys Tyr Asn His Glu Thr Lys Leu
 180 185 190
 Trp Glu Lys Ala
 195

<210> 377
 <211> 330
 <212> PRT
 <213> E. Coli

<400> 377

Met Tyr Phe Leu Asn Asp Leu Asn Phe Ser Arg Arg Asp Ala Gly Phe
 1 5 10 15
 Lys Ala Arg Lys Asp Ala Leu Asp Ile Ala Ser Asp Tyr Glu Asn Ile
 20 25 30
 Ser Val Val Asn Ile Pro Leu Trp Gly Gly Val Val Gln Arg Ile Ile
 35 40 45
 Ser Ser Val Lys Leu Ser Thr Phe Leu Cys Gly Leu Glu Asn Lys Asp
 50 55 60
 Val Leu Ile Phe Asn Phe Pro Met Ala Lys Pro Phe Trp His Ile Leu
 65 70 75 80
 Ser Phe Phe His Arg Leu Leu Lys Phe Arg Ile Val Pro Leu Ile His
 85 90 95
 Asp Ile Asp Glu Leu Arg Gly Gly Gly Ser Asp Ser Val Arg Leu
 100 105 110
 Ala Thr Cys Asp Met Val Ile Ser His Asn Pro Gln Met Thr Lys Tyr
 115 120 125
 Leu Ser Lys Tyr Met Ser Gln Asp Lys Ile Lys Asp Ile Lys Ile Phe
 130 135 140
 Asp Tyr Leu Val Ser Ser Asp Val Glu His Arg Asp Val Thr Asp Lys
 145 150 155 160
 Gln Arg Gly Val Ile Tyr Ala Gly Asn Leu Ser Arg His Lys Cys Ser
 165 170 175
 Phe Ile Tyr Thr Glu Gly Cys Asp Phe Thr Leu Phe Gly Val Asn Tyr
 180 185 190
 Glu Asn Lys Asp Asn Pro Lys Tyr Leu Gly Ser Phe Asp Ala Gln Ser
 195 200 205
 Pro Glu Lys Ile Asn Leu Pro Gly Met Gln Phe Gly Leu Ile Trp Asp
 210 215 220
 Gly Asp Ser Val Glu Thr Cys Ser Gly Ala Phe Gly Asp Tyr Leu Lys
 225 230 235 240
 Phe Asn Asn Pro His Lys Thr Ser Leu Tyr Leu Ser Met Glu Leu Pro
 245 250 255
 Val Phe Ile Trp Asp Lys Ala Ala Leu Ala Asp Phe Ile Val Asp Asn
 260 265 270
 Arg Ile Gly Tyr Ala Val Gly Ser Ile Lys Glu Met Gln Glu Ile Val
 275 280 285
 Asp Ser Met Thr Ile Glu Thr Tyr Lys Gln Ile Ser Glu Asn Thr Lys
 290 295 300
 Ile Ile Ser Gln Lys Ile Arg Thr Gly Ser Tyr Phe Arg Asp Val Leu
 305 310 315 320

Glu Glu Val Ile Asp Asp Leu Lys Thr Arg
 325 330

<210> 378
 <211> 388
 <212> PRT
 <213> E. Coli

<400> 378

Met	Ile	Tyr	Leu	Val	Ile	Ser	Val	Phe	Leu	Ile	Thr	Ala	Phe	Ile	Cys
1				5					10					15	
Leu	Tyr	Leu	Lys	Lys	Asp	Ile	Phe	Tyr	Pro	Ala	Val	Cys	Val	Asn	Ile
			20					25					30		
Ile	Phe	Ala	Leu	Val	Leu	Leu	Gly	Tyr	Glu	Ile	Thr	Ser	Asp	Ile	Tyr
		35					40					45			
Ala	Phe	Gln	Leu	Asn	Asp	Ala	Thr	Leu	Ile	Phe	Leu	Leu	Cys	Asn	Val
	50					55					60				
Leu	Thr	Phe	Thr	Leu	Ser	Cys	Leu	Leu	Thr	Glu	Ser	Val	Leu	Asp	Leu
65					70				75					80	
Asn	Ile	Arg	Lys	Val	Asn	Asn	Ala	Ile	Tyr	Ser	Ile	Pro	Ser	Lys	Lys
				85					90					95	
Val	His	Asn	Val	Gly	Leu	Leu	Val	Ile	Ser	Phe	Ser	Met	Ile	Tyr	Ile
			100					105					110		
Cys	Met	Arg	Leu	Ser	Asn	Tyr	Gln	Phe	Gly	Thr	Ser	Leu	Leu	Ser	Tyr
		115					120					125			
Met	Asn	Leu	Ile	Arg	Asp	Ala	Asp	Val	Glu	Asp	Thr	Ser	Arg	Asn	Phe
	130					135					140				
Ser	Ala	Tyr	Met	Gln	Pro	Ile	Ile	Leu	Thr	Thr	Phe	Ala	Leu	Phe	Ile
145					150					155					160
Trp	Ser	Lys	Lys	Phe	Thr	Asn	Thr	Lys	Val	Ser	Lys	Thr	Phe	Thr	Leu
				165					170					175	
Leu	Val	Phe	Ile	Val	Phe	Ile	Phe	Ala	Ile	Ile	Leu	Asn	Thr	Gly	Lys
			180					185					190		
Gln	Ile	Val	Phe	Met	Val	Ile	Ile	Ser	Tyr	Ala	Phe	Ile	Val	Gly	Val
		195					200					205			
Asn	Arg	Val	Lys	His	Tyr	Val	Tyr	Leu	Ile	Thr	Ala	Val	Gly	Val	Leu
	210					215					220				
Phe	Ser	Leu	Tyr	Met	Leu	Phe	Leu	Arg	Gly	Leu	Pro	Gly	Gly	Met	Ala
225					230					235				240	
Tyr	Tyr	Leu	Ser	Met	Tyr	Leu	Val	Ser	Pro	Ile	Ile	Ala	Phe	Gln	Glu
				245					250					255	
Phe	Tyr	Phe	Gln	Gln	Val	Ser	Asn	Ser	Ala	Ser	Ser	His	Val	Phe	Trp
			260					265					270		
Phe	Phe	Glu	Arg	Leu	Met	Gly	Leu	Leu	Thr	Gly	Gly	Val	Ser	Met	Ser
		275					280					285			
Leu	His	Lys	Glu	Phe	Val	Trp	Val	Gly	Leu	Pro	Thr	Asn	Val	Tyr	Thr
	290					295					300				
Ala	Phe	Ser	Asp	Tyr	Val	Tyr	Ile	Ser	Ala	Glu	Leu	Ser	Tyr	Leu	Met
305					310					315					320
Met	Val	Ile	His	Gly	Cys	Ile	Ser	Gly	Val	Leu	Trp	Arg	Leu	Ser	Arg
				325					330					335	
Asn	Tyr	Ile	Ser	Val	Lys	Ile	Phe	Tyr	Ser	Tyr	Phe	Ile	Tyr	Thr	Phe
			340					345					350		
Ser	Phe	Ile	Phe	Tyr	His	Glu	Ser	Phe	Met	Thr	Asn	Ile	Ser	Ser	Trp
		355				360						365			
Ile	Gln	Ile	Thr	Leu	Cys	Ile	Ile	Val	Phe	Ser	Gln	Phe	Leu	Lys	Ala

370
Gln Lys Ile Lys
385

375

380

<210> 379
<211> 367
<212> PRT
<213> E. Coli

<400> 379

Met	Tyr	Asp	Tyr	Ile	Ile	Val	Gly	Ser	Gly	Leu	Phe	Gly	Ala	Val	Cys
1				5					10					15	
Ala	Asn	Glu	Leu	Lys	Lys	Leu	Asn	Lys	Lys	Val	Leu	Val	Ile	Glu	Lys
			20					25					30		
Arg	Asn	His	Ile	Gly	Gly	Asn	Ala	Tyr	Thr	Glu	Asp	Cys	Glu	Gly	Ile
	35					40						45			
Gln	Ile	His	Lys	Tyr	Gly	Ala	His	Ile	Phe	His	Thr	Asn	Asp	Lys	Tyr
	50					55					60				
Ile	Trp	Asp	Tyr	Val	Asn	Asp	Leu	Val	Glu	Phe	Asn	Arg	Phe	Thr	Asn
65					70					75					80
Ser	Pro	Leu	Ala	Ile	Tyr	Lys	Asp	Lys	Leu	Phe	Asn	Leu	Pro	Phe	Asn
				85					90					95	
Met	Asn	Thr	Phe	His	Gln	Met	Trp	Gly	Val	Lys	Asp	Pro	Gln	Glu	Ala
			100					105					110		
Gln	Asn	Ile	Ile	Asn	Ala	Gln	Lys	Lys	Lys	Tyr	Gly	Asp	Lys	Val	Pro
	115					120						125			
Glu	Asn	Leu	Glu	Glu	Gln	Ala	Ile	Ser	Leu	Val	Gly	Glu	Asp	Leu	Tyr
	130					135					140				
Gln	Ala	Leu	Ile	Lys	Gly	Tyr	Thr	Glu	Lys	Gln	Trp	Gly	Arg	Ser	Ala
145					150					155					160
Lys	Glu	Leu	Pro	Ala	Phe	Ile	Ile	Lys	Arg	Ile	Pro	Val	Arg	Phe	Thr
				165					170					175	
Phe	Asp	Asn	Asn	Tyr	Phe	Ser	Asp	Arg	Tyr	Gln	Gly	Ile	Pro	Val	Gly
		180						185					190		
Gly	Tyr	Thr	Lys	Leu	Ile	Glu	Lys	Met	Leu	Glu	Gly	Val	Asp	Val	Lys
	195						200					205			
Leu	Gly	Ile	Asp	Phe	Leu	Lys	Asp	Lys	Asp	Ser	Leu	Ala	Ser	Lys	Ala
	210					215					220				
His	Arg	Ile	Ile	Tyr	Thr	Gly	Pro	Ile	Asp	Gln	Tyr	Phe	Asp	Tyr	Arg
225					230					235					240
Phe	Gly	Ala	Leu	Glu	Tyr	Arg	Ser	Leu	Lys	Phe	Glu	Thr	Glu	Arg	His
				245					250					255	
Glu	Phe	Pro	Asn	Phe	Gln	Gly	Asn	Ala	Val	Ile	Asn	Phe	Thr	Asp	Ala
			260					265					270		
Asn	Val	Pro	Tyr	Thr	Arg	Ile	Ile	Glu	His	Lys	His	Phe	Asp	Tyr	Val
	275						280						285		
Glu	Thr	Lys	His	Thr	Val	Val	Thr	Lys	Glu	Tyr	Pro	Leu	Glu	Trp	Lys
	290					295					300				
Val	Gly	Asp	Glu	Pro	Tyr	Tyr	Pro	Val	Asn	Asp	Asn	Lys	Asn	Met	Glu
305					310					315					320
Leu	Phe	Lys	Lys	Tyr	Arg	Glu	Leu	Ala	Ser	Arg	Glu	Asp	Lys	Val	Ile
				325					330					335	
Phe	Gly	Gly	Arg	Leu	Ala	Glu	Tyr	Lys	Tyr	Tyr	Asp	Met	His	Gln	Val
			340					345					350		
Ile	Ser	Ala	Ala	Leu	Tyr	Gln	Val	Lys	Asn	Ile	Met	Ser	Thr	Asp	

355

360

365

<210> 380

<211> 371

<212> PRT

<213> E. Coli

<400> 380

Met	Phe	Pro	Lys	Ile	Met	Asn	Asp	Glu	Asn	Phe	Phe	Lys	Lys	Ala	Ala
1				5					10					15	
Ala	His	Gly	Glu	Glu	Pro	Pro	Leu	Thr	Pro	Gln	Asn	Glu	His	Gln	Arg
			20					25					30		
Ser	Gly	Leu	Arg	Phe	Ala	Arg	Arg	Val	Arg	Leu	Pro	Arg	Ala	Val	Gly
		35					40					45			
Leu	Ala	Gly	Met	Phe	Leu	Pro	Ile	Ala	Ser	Thr	Leu	Val	Ser	His	Pro
	50					55					60				
Pro	Pro	Gly	Trp	Trp	Trp	Leu	Val	Leu	Val	Gly	Trp	Ala	Phe	Val	Trp
65					70					75					80
Pro	His	Leu	Ala	Trp	Gln	Ile	Ala	Ser	Arg	Ala	Val	Asp	Pro	Leu	Ser
				85					90					95	
Arg	Glu	Ile	Tyr	Asn	Leu	Lys	Thr	Asp	Ala	Val	Leu	Ala	Gly	Met	Trp
			100					105					110		
Val	Gly	Val	Met	Gly	Val	Asn	Val	Leu	Pro	Ser	Thr	Ala	Met	Leu	Met
		115					120					125			
Ile	Met	Cys	Leu	Asn	Leu	Met	Gly	Ala	Gly	Gly	Pro	Arg	Leu	Phe	Val
	130					135					140				
Ala	Gly	Leu	Val	Leu	Met	Val	Val	Ser	Cys	Leu	Val	Thr	Leu	Glu	Leu
145					150					155					160
Thr	Gly	Ile	Thr	Val	Ser	Phe	Asn	Ser	Ala	Pro	Leu	Glu	Trp	Trp	Leu
				165				170						175	
Ser	Leu	Pro	Ile	Ile	Val	Ile	Tyr	Pro	Leu	Leu	Phe	Gly	Trp	Val	Ser
			180					185					190		
Tyr	Gln	Thr	Ala	Thr	Lys	Leu	Ala	Glu	His	Lys	Arg	Arg	Leu	Gln	Val
		195					200					205			
Met	Ser	Thr	Arg	Asp	Gly	Met	Thr	Gly	Val	Tyr	Asn	Arg	Arg	His	Trp
	210					215					220				
Glu	Thr	Met	Leu	Arg	Asn	Glu	Phe	Asp	Asn	Cys	Arg	Arg	His	Asn	Arg
225					230					235					240
Asp	Ala	Thr	Leu	Leu	Ile	Ile	Asp	Ile	Asp	His	Phe	Lys	Ser	Ile	Asn
				245					250					255	
Asp	Thr	Trp	Gly	His	Asp	Val	Gly	Asp	Glu	Ala	Ile	Val	Ala	Leu	Thr
			260					265					270		
Arg	Gln	Leu	Gln	Ile	Thr	Leu	Arg	Gly	Ser	Asp	Val	Ile	Gly	Arg	Phe
		275					280					285			
Gly	Gly	Asp	Glu	Phe	Ala	Val	Ile	Met	Ser	Gly	Thr	Pro	Ala	Glu	Ser
	290					295					300				
Ala	Ile	Thr	Ala	Met	Leu	Arg	Val	His	Glu	Gly	Leu	Asn	Thr	Leu	Arg
305					310					315					320
Leu	Pro	Asn	Thr	Pro	Gln	Val	Thr	Leu	Arg	Ile	Ser	Val	Gly	Val	Ala
				325					330					335	
Pro	Leu	Asn	Pro	Gln	Met	Ser	His	Tyr	Arg	Glu	Trp	Leu	Lys	Ser	Ala
			340					345					350		
Asp	Leu	Ala	Leu	Tyr	Lys	Ala	Lys	Lys	Ala	Gly	Arg	Asn	Arg	Thr	Glu
		355					360					365			
Val	Ala	Ala													
		370													

<210> 381
 <211> 467
 <212> PRT
 <213> E. Coli

<400> 381

Met	Asp	Val	Asn	Val	Asp	Gln	Phe	Asp	Thr	Glu	Ala	Phe	Arg	Thr	Asp
1				5					10					15	
Lys	Leu	Glu	Leu	Thr	Ser	Gly	Asn	Ile	Ala	Asp	His	Asn	Gly	Asn	Val
			20					25					30		
Val	Ser	Gly	Val	Phe	Asp	Ile	His	Ser	Ser	Asp	Tyr	Val	Leu	Asn	Ala
		35					40					45			
Asp	Leu	Val	Asn	Asp	Arg	Thr	Trp	Asp	Thr	Ser	Lys	Ser	Asn	Tyr	Gly
	50					55					60				
Tyr	Gly	Ile	Val	Ala	Met	Asn	Ser	Asp	Gly	His	Leu	Thr	Ile	Asn	Gly
65					70					75				80	
Asn	Gly	Asp	Val	Asp	Asn	Gly	Thr	Glu	Leu	Asp	Asn	Ser	Ser	Val	Asp
				85				90						95	
Asn	Val	Val	Ala	Ala	Thr	Gly	Asn	Tyr	Lys	Val	Arg	Ile	Asp	Asn	Ala
			100					105					110		
Thr	Gly	Ala	Gly	Ala	Ile	Ala	Asp	Tyr	Lys	Asp	Lys	Glu	Ile	Ile	Tyr
		115					120					125			
Val	Asn	Asp	Val	Asn	Ser	Asn	Ala	Thr	Phe	Ser	Ala	Ala	Asn	Lys	Ala
	130					135					140				
Asp	Leu	Gly	Ala	Tyr	Thr	Tyr	Gln	Ala	Glu	Gln	Arg	Gly	Asn	Thr	Val
145					150					155				160	
Val	Leu	Gln	Gln	Met	Glu	Leu	Thr	Asp	Tyr	Ala	Asn	Met	Ala	Leu	Ser
				165					170				175		
Ile	Pro	Ser	Ala	Asn	Thr	Asn	Ile	Trp	Asn	Leu	Glu	Gln	Asp	Thr	Val
			180					185					190		
Gly	Thr	Arg	Leu	Thr	Asn	Ser	Arg	His	Gly	Leu	Ala	Asp	Asn	Gly	Gly
		195					200					205			
Ala	Trp	Val	Ser	Tyr	Phe	Gly	Gly	Asn	Phe	Asn	Gly	Asp	Asn	Gly	Thr
	210					215					220				
Ile	Asn	Tyr	Asp	Gln	Asp	Val	Asn	Gly	Ile	Met	Val	Gly	Val	Asp	Thr
225					230					235				240	
Lys	Ile	Asp	Gly	Asn	Asn	Ala	Lys	Trp	Ile	Val	Gly	Ala	Ala	Ala	Gly
				245					250					255	
Phe	Ala	Lys	Gly	Asp	Met	Asn	Asp	Arg	Ser	Gly	Gln	Val	Asp	Gln	Asp
			260					265					270		
Ser	Gln	Thr	Ala	Tyr	Ile	Tyr	Ser	Ser	Ala	His	Phe	Ala	Asn	Asn	Val
		275					280					285			
Phe	Val	Asp	Gly	Ser	Leu	Ser	Tyr	Ser	His	Phe	Asn	Asn	Asp	Leu	Ser
	290					295					300				
Ala	Thr	Met	Ser	Asn	Gly	Thr	Tyr	Val	Asp	Gly	Ser	Thr	Asn	Ser	Asp
305					310					315				320	
Ala	Trp	Gly	Phe	Gly	Leu	Lys	Ala	Gly	Tyr	Asp	Phe	Lys	Leu	Gly	Asp
				325					330					335	
Ala	Gly	Tyr	Val	Thr	Pro	Tyr	Gly	Ser	Val	Ser	Gly	Leu	Phe	Gln	Ser
			340					345					350		
Gly	Asp	Asp	Tyr	Gln	Leu	Ser	Asn	Asp	Met	Lys	Val	Asp	Gly	Gln	Ser
	355						360					365			
Tyr	Asp	Ser	Met	Arg	Tyr	Glu	Leu	Gly	Val	Asp	Ala	Gly	Tyr	Thr	Phe
	370					375					380				
Thr	Tyr	Ser	Glu	Asp	Gln	Ala	Leu	Thr	Pro	Tyr	Phe	Lys	Leu	Ala	Tyr
385					390					395					400

Val Tyr Asp Asp Ser Asn Asn Asp Asn Asp Val Asn Gly Asp Ser Ile
 405 410 415
 Asp Asn Gly Thr Glu Gly Ser Ala Val Arg Val Gly Leu Gly Thr Gln
 420 425 430
 Phe Ser Phe Thr Lys Asn Phe Ser Ala Tyr Thr Asp Ala Asn Tyr Leu
 435 440 445
 Gly Gly Gly Asp Val Asp Gln Asp Trp Ser Ala Asn Val Gly Val Lys
 450 455 460
 Tyr Thr Trp
 465

<210> 382
 <211> 222
 <212> PRT
 <213> E. Coli

<400> 382
 Met Pro Val Lys Asp Leu Thr Gly Ile Thr Ala Lys Asp Ala Gln Met
 1 5 10 15
 Leu Ser Val Val Lys Pro Leu Gln Glu Phe Gly Lys Leu Asp Lys Cys
 20 25 30
 Leu Ser Arg Tyr Gly Thr Arg Phe Glu Phe Asn Asn Glu Lys Gln Val
 35 40 45
 Ile Phe Ser Ser Asp Val Asn Asn Glu Asp Thr Phe Val Ile Leu Glu
 50 55 60
 Gly Val Ile Ser Leu Arg Arg Glu Glu Asn Val Leu Ile Gly Ile Thr
 65 70 75 80
 Gln Ala Pro Tyr Ile Met Gly Leu Ala Asp Gly Leu Met Lys Asn Asp
 85 90 95
 Ile Pro Tyr Lys Leu Ile Ser Glu Gly Asn Cys Thr Gly Tyr His Leu
 100 105 110
 Pro Ala Lys Gln Thr Ile Thr Leu Ile Glu Gln Asn Gln Leu Trp Arg
 115 120 125
 Asp Ala Phe Tyr Trp Leu Ala Trp Gln Asn Arg Ile Leu Glu Leu Arg
 130 135 140
 Asp Val Gln Leu Ile Gly His Asn Ser Tyr Glu Gln Ile Arg Ala Thr
 145 150 155 160
 Leu Leu Ser Met Ile Asp Trp Asn Glu Glu Leu Arg Ser Arg Ile Gly
 165 170 175
 Val Met Asn Tyr Ile His Gln Arg Thr Arg Ile Ser Arg Ser Val Val
 180 185 190
 Ala Glu Val Leu Ala Ala Leu Arg Lys Gly Gly Tyr Ile Glu Met Asn
 195 200 205
 Lys Gly Lys Leu Val Ala Ile Asn Arg Leu Pro Ser Glu Tyr
 210 215 220

<210> 383
 <211> 84
 <212> PRT
 <213> E. Coli

<400> 383
 Met Thr Asp Lys Ile Arg Thr Leu Gln Gly Arg Val Val Ser Asp Lys
 1 5 10 15

Met Glu Lys Ser Ile Val Val Ala Ile Glu Arg Phe Val Lys His Pro
 20 25 30
 Ile Tyr Gly Lys Phe Ile Lys Arg Thr Thr Lys Leu His Val His Asp
 35 40 45
 Glu Asn Asn Glu Cys Gly Ile Gly Asp Val Val Glu Ile Arg Glu Cys
 50 55 60
 Arg Pro Leu Ser Lys Thr Lys Ser Trp Thr Leu Val Arg Val Val Glu
 65 70 75 80
 Lys Ala Val Leu

<210> 384
 <211> 63
 <212> PRT
 <213> E. Coli

<400> 384

Met Lys Ala Lys Glu Leu Arg Glu Lys Ser Val Glu Glu Leu Asn Thr
 1 5 10 15
 Glu Leu Leu Asn Leu Leu Arg Glu Gln Phe Asn Leu Arg Met Gln Ala
 20 25 30
 Ala Ser Gly Gln Leu Gln Gln Ser His Leu Leu Lys Gln Val Arg Arg
 35 40 45
 Asp Val Ala Arg Val Lys Thr Leu Leu Asn Glu Lys Ala Gly Ala
 50 55 60

<210> 385
 <211> 136
 <212> PRT
 <213> E. Coli

<400> 385

Met Leu Gln Pro Lys Arg Thr Lys Phe Arg Lys Met His Lys Gly Arg
 1 5 10 15
 Asn Arg Gly Leu Ala Gln Gly Thr Asp Val Ser Phe Gly Ser Phe Gly
 20 25 30
 Leu Lys Ala Val Gly Arg Gly Arg Leu Thr Ala Arg Gln Ile Glu Ala
 35 40 45
 Ala Arg Arg Ala Met Thr Arg Ala Val Lys Arg Gln Gly Lys Ile Trp
 50 55 60
 Ile Arg Val Phe Pro Asp Lys Pro Ile Thr Glu Lys Pro Leu Ala Val
 65 70 75 80
 Arg Met Gly Lys Gly Lys Gly Asn Val Glu Tyr Trp Val Ala Leu Ile
 85 90 95
 Gln Pro Gly Lys Val Leu Tyr Glu Met Asp Gly Val Pro Glu Glu Leu
 100 105 110
 Ala Arg Glu Ala Phe Lys Leu Ala Ala Lys Leu Pro Ile Lys Thr
 115 120 125
 Thr Phe Val Thr Lys Thr Val Met
 130 135

<210> 386
 <211> 233
 <212> PRT

<213> E. Coli

<400> 386

Met	Gly	Gln	Lys	Val	His	Pro	Asn	Gly	Ile	Arg	Leu	Gly	Ile	Val	Lys
1				5					10					15	
Pro	Trp	Asn	Ser	Thr	Trp	Phe	Ala	Asn	Thr	Lys	Glu	Phe	Ala	Asp	Asn
			20					25					30		
Leu	Asp	Ser	Asp	Phe	Lys	Val	Arg	Gln	Tyr	Leu	Thr	Lys	Glu	Leu	Ala
		35					40					45			
Lys	Ala	Ser	Val	Ser	Arg	Ile	Val	Ile	Glu	Arg	Pro	Ala	Lys	Ser	Ile
	50					55				60					
Arg	Val	Thr	Ile	His	Thr	Ala	Arg	Pro	Gly	Ile	Val	Ile	Gly	Lys	Lys
65					70					75					80
Gly	Glu	Asp	Val	Glu	Lys	Leu	Arg	Lys	Val	Val	Ala	Asp	Ile	Ala	Gly
				85					90					95	
Val	Pro	Ala	Gln	Ile	Asn	Ile	Ala	Glu	Val	Arg	Lys	Pro	Glu	Leu	Asp
			100					105					110		
Ala	Lys	Leu	Val	Ala	Asp	Ser	Ile	Thr	Ser	Gln	Leu	Glu	Arg	Arg	Val
		115					120					125			
Met	Phe	Arg	Arg	Ala	Met	Lys	Arg	Ala	Val	Gln	Asn	Ala	Met	Arg	Leu
	130					135					140				
Gly	Ala	Lys	Gly	Ile	Lys	Val	Glu	Val	Ser	Gly	Arg	Leu	Gly	Gly	Ala
145					150					155					160
Glu	Ile	Ala	Arg	Thr	Glu	Trp	Tyr	Arg	Glu	Gly	Arg	Val	Pro	Leu	His
				165					170					175	
Thr	Leu	Arg	Ala	Asp	Ile	Asp	Tyr	Asn	Thr	Ser	Glu	Ala	His	Thr	Thr
			180					185					190		
Tyr	Gly	Val	Ile	Gly	Val	Lys	Val	Trp	Ile	Phe	Lys	Gly	Glu	Ile	Leu
	195					200						205			
Gly	Gly	Met	Ala	Ala	Val	Glu	Gln	Pro	Glu	Lys	Pro	Ala	Ala	Gln	Pro
	210					215					220				
Lys	Lys	Gln	Gln	Arg	Lys	Gly	Arg	Lys							
225					230										

<210> 387

<211> 110

<212> PRT

<213> E. Coli

<400> 387

Met	Glu	Thr	Ile	Ala	Lys	His	Arg	His	Ala	Arg	Ser	Ser	Ala	Gln	Lys
1				5					10					15	
Val	Arg	Leu	Val	Ala	Asp	Leu	Ile	Arg	Gly	Lys	Lys	Val	Ser	Gln	Ala
			20					25					30		
Leu	Asp	Ile	Leu	Thr	Tyr	Thr	Asn	Lys	Lys	Ala	Ala	Val	Leu	Val	Lys
		35					40					45			
Lys	Val	Leu	Glu	Ser	Ala	Ile	Ala	Asn	Ala	Glu	His	Asn	Asp	Gly	Ala
	50					55					60				
Asp	Ile	Asp	Asp	Leu	Lys	Val	Thr	Lys	Ile	Phe	Val	Asp	Glu	Gly	Pro
65					70					75					80
Ser	Met	Lys	Arg	Ile	Met	Pro	Arg	Ala	Lys	Gly	Arg	Ala	Asp	Arg	Ile
				85					90					95	
Leu	Lys	Arg	Thr	Ser	His	Ile	Thr	Val	Val	Val	Ser	Asp	Arg		
			100					105					110		

<210> 388
 <211> 92
 <212> PRT
 <213> E. Coli

<400> 388
 Met Pro Arg Ser Leu Lys Lys Gly Pro Phe Ile Asp Leu His Leu Leu
 1 5 10 15
 Met Lys Val Glu Lys Ala Val Glu Ser Gly Asp Lys Lys Pro Leu Arg
 20 25 30
 Thr Trp Ser Arg Arg Ser Thr Ile Phe Pro Asn Met Ile Gly Leu Thr
 35 40 45
 Ile Ala Val His Asn Gly Arg Gln His Val Pro Val Phe Val Thr Asp
 50 55 60
 Glu Met Val Gly His Lys Leu Gly Glu Phe Ala Pro Thr Arg Thr Tyr
 65 70 75 80
 Arg Gly His Ala Ala Asp Lys Lys Ala Lys Lys Lys
 85 90

<210> 389
 <211> 273
 <212> PRT
 <213> E. Coli

<400> 389
 Met Ala Val Val Lys Cys Lys Pro Thr Ser Pro Gly Arg Arg His Val
 1 5 10 15
 Val Lys Val Val Asn Pro Glu Leu His Lys Gly Lys Pro Phe Ala Pro
 20 25 30
 Leu Leu Glu Lys Asn Ser Lys Ser Gly Gly Arg Asn Asn Gly Arg
 35 40 45
 Ile Thr Thr Arg His Ile Gly Gly Gly His Lys Gln Ala Tyr Arg Ile
 50 55 60
 Val Asp Phe Lys Arg Asn Lys Asp Gly Ile Pro Ala Val Val Glu Arg
 65 70 75 80
 Leu Glu Tyr Asp Pro Asn Arg Ser Ala Asn Ile Ala Leu Val Leu Tyr
 85 90 95
 Lys Asp Gly Glu Arg Arg Tyr Ile Leu Ala Pro Lys Gly Leu Lys Ala
 100 105 110
 Gly Asp Gln Ile Gln Ser Gly Val Asp Ala Ala Ile Lys Pro Gly Asn
 115 120 125
 Thr Leu Pro Met Arg Asn Ile Pro Val Gly Ser Thr Val His Asn Val
 130 135 140
 Glu Met Lys Pro Gly Lys Gly Gly Gln Leu Ala Arg Ser Ala Gly Thr
 145 150 155 160
 Tyr Val Gln Ile Val Ala Arg Asp Gly Ala Tyr Val Thr Leu Arg Leu
 165 170 175
 Arg Ser Gly Glu Met Arg Lys Val Glu Ala Asp Cys Arg Ala Thr Leu
 180 185 190
 Gly Glu Val Gly Asn Ala Glu His Met Leu Arg Val Leu Gly Lys Ala
 195 200 205
 Gly Ala Ala Arg Trp Arg Gly Val Arg Pro Thr Val Arg Gly Thr Ala
 210 215 220

Met Asn Pro Val Asp His Pro His Gly Gly Gly Glu Gly Arg Asn Phe
 225 230 235 240
 Gly Lys His Pro Val Thr Pro Trp Gly Val Gln Thr Lys Gly Lys Lys
 245 250 255
 Thr Arg Ser Asn Lys Arg Thr Asp Lys Phe Ile Val Arg Arg Arg Ser
 260 265 270
 Lys

<210> 390
 <211> 100
 <212> PRT
 <213> E. Coli

<400> 390
 Met Ile Arg Glu Glu Arg Leu Leu Lys Val Leu Arg Ala Pro His Val
 1 5 10 15
 Ser Glu Lys Ala Ser Thr Ala Met Glu Lys Ser Asn Thr Ile Val Leu
 20 25 30
 Lys Val Ala Lys Asp Ala Thr Lys Ala Glu Ile Lys Ala Ala Val Gln
 35 40 45
 Lys Leu Phe Glu Val Glu Val Glu Val Val Asn Thr Leu Val Val Lys
 50 55 60
 Gly Lys Val Lys Arg His Gly Gln Arg Ile Gly Arg Arg Ser Asp Trp
 65 70 75 80
 Lys Lys Ala Tyr Val Thr Leu Lys Glu Gly Gln Asn Leu Asp Phe Val
 85 90 95
 Gly Gly Ala Glu
 100

<210> 391
 <211> 201
 <212> PRT
 <213> E. Coli

<400> 391
 Met Glu Leu Val Leu Lys Asp Ala Gln Ser Ala Leu Thr Val Ser Glu
 1 5 10 15
 Thr Thr Phe Gly Arg Asp Phe Asn Glu Ala Leu Val His Gln Val Val
 20 25 30
 Val Ala Tyr Ala Ala Gly Ala Arg Gln Gly Thr Arg Ala Gln Lys Thr
 35 40 45
 Arg Ala Glu Val Thr Gly Ser Gly Lys Lys Pro Trp Arg Gln Lys Gly
 50 55 60
 Thr Gly Arg Ala Arg Ser Gly Ser Ile Lys Ser Pro Ile Trp Arg Ser
 65 70 75 80
 Gly Gly Val Thr Phe Ala Ala Arg Pro Gln Asp His Ser Gln Lys Val
 85 90 95
 Asn Lys Lys Met Tyr Arg Gly Ala Leu Lys Ser Ile Leu Ser Glu Leu
 100 105 110
 Val Arg Gln Asp Arg Leu Ile Val Val Glu Lys Phe Ser Val Glu Ala
 115 120 125
 Pro Lys Thr Lys Leu Leu Ala Gln Lys Leu Lys Asp Met Ala Leu Glu

Leu Ile Asp Gln Ala Thr Ala Glu Ile Val Glu Thr Ala Lys Arg Thr
 20 25 30
 Gly Ala Gln Val Arg Gly Pro Ile Pro Leu Pro Thr Arg Lys Glu Arg
 35 40 45
 Phe Thr Val Leu Ile Ser Pro His Val Asn Lys Asp Ala Arg Asp Gln
 50 55 60
 Tyr Glu Ile Arg Thr His Leu Arg Leu Val Asp Ile Val Glu Pro Thr
 65 70 75 80
 Glu Lys Thr Val Asp Ala Leu Met Arg Leu Asp Leu Ala Ala Gly Val
 85 90 95
 Asp Val Gln Ile Ser Leu Gly
 100

<210> 394
 <211> 118
 <212> PRT
 <213> E. Coli

<400> 394

Met Ala Arg Val Lys Arg Gly Val Ile Ala Arg Ala Arg His Lys Lys
 1 5 10 15
 Ile Leu Lys Gln Ala Lys Gly Tyr Tyr Gly Ala Arg Ser Arg Val Tyr
 20 25 30
 Arg Val Ala Phe Gln Ala Val Ile Lys Ala Gly Gln Tyr Ala Tyr Arg
 35 40 45
 Asp Arg Arg Gln Arg Lys Arg Gln Phe Arg Gln Leu Trp Ile Ala Arg
 50 55 60
 Ile Asn Ala Ala Ala Arg Gln Asn Gly Ile Ser Tyr Ser Lys Phe Ile
 65 70 75 80
 Asn Gly Leu Lys Lys Ala Ser Val Glu Ile Asp Arg Lys Ile Leu Ala
 85 90 95
 Asp Ile Ala Val Phe Asp Lys Val Ala Phe Thr Ala Leu Val Glu Lys
 100 105 110
 Ala Lys Ala Ala Leu Ala
 115

<210> 395
 <211> 65
 <212> PRT
 <213> E. Coli

<400> 395

Met Pro Lys Ile Lys Thr Val Arg Gly Ala Ala Lys Arg Phe Lys Lys
 1 5 10 15
 Thr Gly Lys Gly Gly Phe Lys His Lys His Ala Asn Leu Arg His Ile
 20 25 30
 Leu Thr Lys Lys Ala Thr Lys Arg Lys Arg His Leu Arg Pro Lys Ala
 35 40 45
 Met Val Ser Lys Gly Asp Leu Gly Leu Val Ile Ala Cys Leu Pro Tyr
 50 55 60
 Ala
 65

002210" 50225450

<210> 396
 <211> 180
 <212> PRT
 <213> E. Coli

<400> 396
 Met Lys Gly Gly Lys Arg Val Gln Thr Ala Arg Pro Asn Arg Ile Asn
 1 5 10 15
 Gly Glu Ile Arg Ala Gln Glu Val Arg Leu Thr Gly Leu Glu Gly Glu
 20 25 30
 Gln Leu Gly Ile Val Ser Leu Arg Glu Ala Leu Glu Lys Ala Glu Glu
 35 40 45
 Ala Gly Val Asp Leu Val Glu Ile Ser Pro Asn Ala Glu Pro Pro Val
 50 55 60
 Cys Arg Ile Met Asp Tyr Gly Lys Phe Leu Tyr Glu Lys Ser Lys Ser
 65 70 75 80
 Ser Lys Glu Gln Lys Lys Lys Gln Lys Val Ile Gln Val Lys Glu Ile
 85 90 95
 Lys Phe Arg Pro Gly Thr Asp Glu Gly Asp Tyr Gln Val Lys Leu Arg
 100 105 110
 Ser Leu Ile Arg Phe Leu Glu Glu Gly Asp Lys Ala Lys Ile Thr Leu
 115 120 125
 Arg Phe Arg Gly Arg Glu Met Ala His Gln Gln Ile Gly Met Glu Val
 130 135 140
 Leu Asn Arg Val Lys Asp Asp Leu Gln Glu Leu Ala Val Val Glu Ser
 145 150 155 160
 Phe Pro Thr Lys Ile Glu Gly Arg Gln Met Ile Met Val Leu Ala Pro
 165 170 175
 Lys Lys Lys Gln
 180

<210> 397
 <211> 642
 <212> PRT
 <213> E. Coli

<400> 397
 Met Pro Val Ile Thr Leu Pro Asp Gly Ser Gln Arg His Tyr Asp His
 1 5 10 15
 Ala Val Ser Pro Met Asp Val Ala Leu Asp Ile Gly Pro Gly Leu Ala
 20 25 30
 Lys Ala Cys Ile Ala Gly Arg Val Asn Gly Glu Leu Val Asp Ala Cys
 35 40 45
 Asp Leu Ile Glu Asn Asp Ala Gln Leu Ser Ile Ile Thr Ala Lys Asp
 50 55 60
 Glu Glu Gly Leu Glu Ile Arg His Ser Cys Ala His Leu Leu Gly
 65 70 75 80
 His Ala Ile Lys Gln Leu Trp Pro His Thr Lys Met Ala Ile Gly Pro
 85 90 95
 Val Ile Asp Asn Gly Phe Tyr Tyr Asp Val Asp Leu Asp Arg Thr Leu
 100 105 110
 Thr Gln Glu Asp Val Glu Ala Leu Glu Lys Arg Met His Glu Leu Ala
 115 120 125
 Glu Lys Asn Tyr Asp Val Ile Lys Lys Lys Val Ser Trp His Glu Ala

130		135		140
Arg Glu Thr Phe Ala Asn Arg Gly Glu Ser Tyr Lys Val Ser Ile Leu				
145		150		155
Asp Glu Asn Ile Ala His Asp Asp Lys Pro Gly Leu Tyr Phe His Glu				
	165		170	175
Glu Tyr Val Asp Met Cys Arg Gly Pro His Val Pro Asn Met Arg Phe				
	180		185	190
Cys His His Phe Lys Leu Met Lys Thr Ala Gly Ala Tyr Trp Arg Gly				
	195	200		205
Asp Ser Asn Asn Lys Met Leu Gln Arg Ile Tyr Gly Thr Ala Trp Ala				
210		215		220
Asp Lys Lys Ala Leu Asn Ala Tyr Leu Gln Arg Leu Glu Glu Ala Ala				
225		230		235
Lys Arg Asp His Arg Lys Ile Gly Lys Gln Leu Asp Leu Tyr His Met				
	245		250	255
Gln Glu Glu Ala Pro Gly Met Val Phe Trp His Asn Asp Gly Trp Thr				
	260		265	270
Ile Phe Arg Glu Leu Glu Val Phe Val Arg Ser Lys Leu Lys Glu Tyr				
	275		280	285
Gln Tyr Gln Glu Val Lys Gly Pro Phe Met Met Asp Arg Val Leu Trp				
290		295		300
Glu Lys Thr Gly His Trp Asp Asn Tyr Lys Asp Ala Met Phe Thr Thr				
305		310		315
Ser Ser Glu Asn Arg Glu Tyr Cys Ile Lys Pro Met Asn Cys Pro Gly				
	325		330	335
His Val Gln Ile Phe Asn Gln Gly Leu Lys Ser Tyr Arg Asp Leu Pro				
	340		345	350
Leu Arg Met Ala Glu Phe Gly Ser Cys His Arg Asn Glu Pro Ser Gly				
	355		360	365
Ser Leu His Gly Leu Met Arg Val Arg Gly Phe Thr Gln Asp Asp Ala				
370		375		380
His Ile Phe Cys Thr Glu Glu Gln Ile Arg Asp Glu Val Asn Gly Cys				
385		390		395
Ile Arg Leu Val Tyr Asp Met Tyr Ser Thr Phe Gly Phe Glu Lys Ile				
	405		410	415
Val Val Lys Leu Ser Thr Arg Pro Glu Lys Arg Ile Gly Ser Asp Glu				
	420		425	430
Met Trp Asp Arg Ala Glu Ala Asp Leu Ala Val Ala Leu Glu Glu Asn				
	435		440	445
Asn Ile Pro Phe Glu Tyr Gln Leu Gly Glu Gly Ala Phe Tyr Gly Pro				
450		455		460
Lys Ile Glu Phe Thr Leu Tyr Asp Cys Leu Asp Arg Ala Trp Gln Cys				
465		470		475
Gly Thr Val Gln Leu Asp Phe Ser Leu Pro Ser Arg Leu Ser Ala Ser				
	485		490	495
Tyr Val Gly Glu Asp Asn Glu Arg Lys Val Pro Val Met Ile His Arg				
	500		505	510
Ala Ile Leu Gly Ser Met Glu Arg Phe Ile Gly Ile Leu Thr Glu Glu				
	515		520	525
Phe Ala Gly Phe Phe Pro Thr Trp Leu Ala Pro Val Gln Val Val Ile				
530		535		540
Met Asn Ile Thr Asp Ser Gln Ser Glu Tyr Val Asn Glu Leu Thr Gln				
545		550		555
Lys Leu Ser Asn Ala Gly Ile Arg Val Lys Ala Asp Leu Arg Asn Glu				
	565		570	575
Lys Ile Gly Phe Lys Ile Arg Glu His Thr Leu Arg Arg Val Pro Tyr				
	580		585	590

Met	Leu	Val	Cys	Gly	Asp	Lys	Glu	Val	Glu	Ser	Gly	Lys	Val	Ala	Val
		595					600					605			
Arg	Thr	Arg	Arg	Gly	Lys	Asp	Leu	Gly	Ser	Met	Asp	Val	Asn	Glu	Val
	610					615					620				
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Glu	Glu														

<210> 398
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 <212> PRT
 <213> E. Coli

<400> 398

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Ile	Ala	Ser	Ile	Asn	Arg	Ala	Ala	Met	Tyr	Gly	Gln	Lys	Cys	Ala	Leu
			20					25					30		
Ile	Glu	Ala	Lys	Glu	Leu	Gly	Gly	Thr	Cys	Val	Asn	Val	Gly	Cys	Val
		35					40					45			
Pro	Lys	Lys	Val	Met	Trp	His	Ala	Ala	Gln	Ile	Arg	Glu	Ala	Ile	His
	50					55					60				
Met	Tyr	Gly	Pro	Asp	Tyr	Gly	Phe	Asp	Thr	Thr	Ile	Asn	Lys	Phe	Asn
65				70						75					80
Trp	Glu	Thr	Leu	Ile	Ala	Ser	Arg	Thr	Ala	Tyr	Ile	Asp	Arg	Ile	His
			85						90					95	
Thr	Ser	Tyr	Glu	Asn	Val	Leu	Gly	Lys	Asn	Asn	Val	Asp	Val	Ile	Lys
			100					105					110		
Gly	Phe	Ala	Arg	Phe	Val	Asp	Ala	Lys	Thr	Leu	Glu	Val	Asn	Gly	Glu
		115					120					125			
Thr	Ile	Thr	Ala	Asp	His	Ile	Leu	Ile	Ala	Thr	Gly	Gly	Arg	Pro	Ser
	130					135						140			
His	Pro	Asp	Ile	Pro	Gly	Val	Glu	Tyr	Gly	Ile	Asp	Ser	Asp	Gly	Phe
145					150					155					160
Phe	Ala	Leu	Pro	Ala	Leu	Pro	Glu	Arg	Val	Ala	Val	Val	Gly	Ala	Gly
			165						170					175	
Tyr	Ile	Ala	Val	Glu	Leu	Ala	Gly	Val	Ile	Asn	Gly	Leu	Gly	Ala	Lys
			180				185						190		
Thr	His	Leu	Phe	Val	Arg	Lys	His	Ala	Pro	Leu	Arg	Ser	Phe	Asp	Pro
	195						200					205			
Met	Ile	Ser	Glu	Thr	Leu	Val	Glu	Val	Met	Asn	Ala	Glu	Gly	Pro	Gln
	210					215					220				
Leu	His	Thr	Asn	Ala	Ile	Pro	Lys	Ala	Val	Val	Lys	Asn	Thr	Asp	Gly
225					230					235					240
Ser	Leu	Thr	Leu	Glu	Leu	Glu	Asp	Gly	Arg	Ser	Glu	Thr	Val	Asp	Cys
			245						250					255	
Leu	Ile	Trp	Ala	Ile	Gly	Arg	Glu	Pro	Ala	Asn	Asp	Asn	Ile	Asn	Leu
		260						265					270		
Glu	Ala	Ala	Gly	Val	Lys	Thr	Asn	Glu	Lys	Gly	Tyr	Ile	Val	Val	Asp
		275					280					285			
Lys	Tyr	Gln	Asn	Thr	Asn	Ile	Glu	Gly	Ile	Tyr	Ala	Val	Gly	Asp	Asn
	290					295					300				
Thr	Gly	Ala	Val	Glu	Leu	Thr	Pro	Val	Ala	Val	Ala	Ala	Gly	Arg	Arg
305					310					315					320
Leu	Ser	Glu	Arg	Leu	Phe	Asn	Asn	Lys	Pro	Asp	Glu	His	Leu	Asp	Tyr

004220"5042460

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ccgguauucg	caguungcau	cgguuggua	agucgggaug	accccuugc	cgaaacagug	2040
cucuaccccc	ggagaugaau	ucacgagggc	cuaccuaaa	agcuuucggg	gagaaccagc	2100
uauccccgg	uuugauuggc	cuuucacccc	cagccacaag	ucauccgcua	auuuuucaac	2160
auuagucggu	ucgguccucc	aguuauguu	acccaaccuu	caaccugccc	auggcuaagau	2220
caccggguuu	cgggucuaa	cccugcaacu	uaacgcccag	uuaagacucg	guuucccuuc	2280
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ugucgaaaca	cacugggguu	ccccauucgg	aaaucgccc	uuauaacggu	ucauauacc	2820
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<210> 400
 <211> 120
 <212> RNA
 <213> E. Coli

<400> 400

augccuggca	guucccuacu	cucgcauggg	gagacccac	acuaccaucg	gcgcuacggc	60
guuucacuuc	ugaguucggc	auggggucag	gugggaccac	cgcgcuacgg	ccgccaggca	120

<210> 401
 <211> 76
 <212> RNA
 <213> E. Coli

<400> 401

gucccuucg	ucuagaggcc	caggacaccg	cccuuucacg	gcgguaacag	ggguucgaau	60
cccuagggg	acgcca					76

<210> 402
 <211> 1549
 <212> RNA
 <213> E. Coli

<400> 402

aaauugaaga	guuugaucan	ggcucagauu	gaacgcuggc	ggcaggccua	acacaugcaa	60
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ugucugggaa	gcugccugau	ggagggggau	aacuacugga	aacgguaagcu	aaauaccgau	180
aaugucgcaa	gaccaaagag	ggggaccuuc	gggccucuuu	ccaucggaug	ugcccagaug	240
ggauuagcuu	guuggugggg	uaacggcuca	ccaaggcgac	gaucuccuagc	uggucugaga	300
ggaugaccag	ccacacugga	acugagacac	gguccagacu	ccuacgggag	gcagcagugg	360
ggaauauugc	acaauuggcg	caagccugau	gcagccaugc	cgcguguaug	aagaaggccu	420
ucggguugua	aaguacuuuc	agcggggagg	aagggaguaa	aguuaauacc	uuugcucauu	480

gacguuaccc	gcagaagaag	caccggcuaa	cuccgugcca	gcagccgcgg	uaauacggag	540
ggugcaagcg	uuaaucggaa	uuacugggcg	uaaagcgcac	gcagcggggu	ugguuaaguc	600
agaugugaaa	uccccgggcu	caaccuggga	acugcaucug	auacuggcaa	gcuugagucu	660
cguagagggg	gguagaauuc	cagguguagc	ggugaaaugc	guagagaucu	ggaggaauac	720
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aagguaaaaa	cucaaaugaa	uugacggggg	cccgacacaag	cgguggagca	ugugguuuaa	960
uucgaugcaa	cgcgaagaac	cuuaccuggu	cuugacaucc	acggaaguuu	ucagagauga	1020
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caucauggcc	cuuacgacca	gggcuacaca	cgugcuacaa	uggcgcauac	aaagagaagc	1260
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uucccgggcc	uuguacacac	cgcccgcac	accaugggag	uggguugcaa	aagaaguagg	1440
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<210> 403
 <211> 17
 <212> DNA
 <213> Artificial
 <220>
 <223> Primer Oligonucleotide

<400> 403	
tgtttatcag accgctt	17

<210> 404
 <211> 18
 <212> DNA
 <213> Artificial
 <220>
 <223> Primer Oligonucleotide

<400> 404	
acaatttcac acagcctc	18

<210> 405
 <211> 159
 <212> DNA
 <213> Escherichia coli

<400> 405	
caggtggtat ggaaacccaa aatggagacg ggaagctgaa ccagatagtt actggaggtg	60
atcaccagca gatgaaataa cgataaccag aacaacgcct tatagcgttg agtttgcgag	120
aaaacgttca tattgtacct ttttgattaa ccattgggg	159

<210> 406
 <211> 640
 <212> DNA
 <213> Escherichia coli


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<220>
<221> misc_feature
<222> (1)...(640)
<223> n = A,T,C or G

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ggggnccaaa gtgtttgggn cgggcaactg gaggccaaacc ttaanttngg ggaaatTTTT      60
aanaaaaggc ggggatttgt nagccacggg ngattanttt anaataaatt aagtgttgcc      120
ataaggggac aaagngaagg aagtggntat taanggannc gccaatgcga nttagggcag      180
accattcggc cattcgccctt cttgggttatc gaagttcatc cagatagccg ttgccngacc      240
gaccagattc gcttcnggca caaagcccca gtaaogggctg tccgcgctgt tgtcgcggtt      300
gtcgcccatc atgaagtatt gtcccggagg aacaatccag gttgccagtt gttgccctgg      360
ctgctggtaa tacatcccca cctgatcctg cgcaatcggc actgtcagaa tgcggtgcgt      420
cacatcacc cagtgctctt tacgctcgga aagacgaatt ccattttctt tggtttcggt      480
tttcggcact tcaaaagaatc cgctggtcgc ttccccacca ttacggcggtg agaaggtctg      540
aacgaaatcg ctcggttcca cgtttgagta ggtgaccggc agcgcggttt cacacgcctg      600
gccggaactg catcccgggt gaatcgtcag ctcttttgag      640

<210> 407
<211> 682
<212> DNA
<213> Escherichia coli

<220>
<221> misc_feature
<222> (1)...(682)
<223> n = A,T,C or G

<400> 407
cctgcagggt aatgtcgcca ttaaactggc gcaggcagcc aaagagttgc tccgcttcta      60
cccagtcggc agcgacaact tgcgttaaag tcgcaaaatt atcatctgca ctactgcgt      120
gacgtaagcg gatggagtg cgggaaacct catagtgacc gccaccaggt tggcctgcgt      180
cgctttgtag cgtacgcgcg gcattggcaa taagattcag atactcagac tcttcggggg      240
ccttcgccag cataaaaagag gaggatgctc gcgtatgcag caactgctcc agcgcaaatt      300
gcagccgcgg ttgagtatca ctgaataaag gatcgtttcc gtcaatcaaa tgtggctgag      360
caaatatttc ctgatagcta tcggtatcag gaaccaggtc acgccatgca agtttcgtaa      420
tgggtcaaagt tgatgttttt tagtctgttg tcaaagccgc nattataccn gtaaccggca      480
ctacagcaca cgtagaaagc acccgacaat actcctggca tgggcgttaa agctcacagg      540
atggagatct tttcttcact ggcctaaaaa gctgatattc tgtaaagagt tacacngtaa      600
cattgagatc gctatgaaat atcaacaact tggaaaatct tgnaaagcng gttggaaaat      660
ggaaagtatc tgggttaagaa gc      682

<210> 408
<211> 309
<212> DNA
<213> Escherichia coli

<400> 408
ggggatccgg cagaatttta cgctgaccaa tgacgcgacg acgtggcatg gaaataactcc      60
gttggttaatt caggattgtc caaaactcta cgagtttagt ttgacattta agttaaaacg      120
tttggcctta cttaacggag aaccattaag ccttaggacg cttcacgcca tacttggaaac      180
gagcctgctt acggtcttta acgcccggag agtcaagcgc accacgtacg gtgtggtaac      240
gaacacccgg gaggtcttta acacgaccgc cacggatcag gatcacggag tgctcctgca      300
gccaaagctt      309

<210> 409
<211> 1167

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<223> n = A,T,C or G

<400> 412

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gaaaatggaa	cactttccgc	aatgcctgtt	gctatcacgc	ttaamccatt	tcattg	cgat	120
ttacacagaa	cggacgtcct	gtcgcagtat	attaagtcgt	cgatagaaac	aagcattgaa		180
aggcacagca	gtagtcaaac	agtgtgaaac	gctactggcg	ccttacagcg	caaaaaggct		240
ggtgactaaa	aagtcaccag	ccatcagcct	gattttctcag	gctgcaaccg	gaagggttgg		300
cttattttaac	ttcaacttca	gogccagctt	cttccagagc	ttttttcagt	gcttctgcgt		360
cgtcttttgc	cacgccttct	ttcagagcag	ccgggtgcag	attctaccag	gtcttttagct		420
tcttttcagac	ccaggccagt	tgcgccacgt	actgctttga	taacagcaac	tttgtttagcg		480
ccagcagctt	tcagaattac	gtcgaattca	agttttttct	tcagcagctt	caaccggggc		540
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tcaagttcta	caacgtccat	tacagacata	gctgcaactg	cttcaatgat	tkgatcttwa		660
gtgatagaca	tttaaattgt	tcctgaatat	cagaataagt	ttatacgtaa	gcgaatgcgt		720
taaaaagata	actgcgatta	agcagcttct	ttcgcacgcg	gtacagcagc	cagaggtcga		780
accagtttgc	cagccgaagg	ttggcttttc	agcctnnncn	natta			825

<210> 413

<211> 425

<212> DNA

<213> Escherichia coli

<400> 413

agtagtcaaa	caggtgkgra	acgctactgg	cgccttacag	cgcaaaaagg	ctggtgacta	60
aaaagtcaacc	agccatcacc	ctgatttctc	aggctgcaac	ccggaagggt	tggttatttt	120
aacttcaact	tcagcgccag	cttcttccag	agcttttttc	agtgtctctg	cgctgtcttt	180
gtcacgcct	tcttttcagag	cagccgggtgc	agattctacc	aggtcttttag	cttctttcag	240
accaggcca	gttgcgccac	gtactgcttt	gataacagca	actttgttag	cgccagcagc	300
tttcagaatt	acgtcgaatt	cagttttttc	ttcagcagct	tcaaccgggc	cagcagctac	360
agctacagca	gcagcagcgg	aaacacccga	atttttcttc	cattgcagag	atcaagttct	420
acaac						425

<210> 414

<211> 126

<212> DNA

<213> Escherichia coli

<400> 414

agagcttttt	tcagtgtctc	tgcgtcgtct	ttgctcacgc	cttcttttcag	agcagccggg	60
gcagattcta	ccaggctttt	agcttctttc	agaccagggc	cagttgcgcc	acgtactgct	120
ttrata						126

<210> 415

<211> 264

<212> DNA

<213> Escherichia coli

<400> 415

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ttttttcaag	tgcttctgcg	tcgtcttttc	tcacgccttc	tttcagagca	gccgggtgcag	120
attctaccag	gtcttttagct	tctttcagac	ccaggccagt	tgcgccacgt	actgctttga	180
taacagcaac	tttggttagcg	ccagcagctt	tcagaattac	gtcgaattca	gttttttctt	240
cagcagcttc	aaccggggcca	gcag				264

<210> 416

<211> 201

Figure 1 consists of 12 sub-graphs, each representing a different fish species. Each graph plots the percentage of total catch (Y-axis, 0 to 100) against time (X-axis, 1980 to 1990). Three fishing methods are compared: 100% gillnet (solid line), 100% trawl (dashed line), and 50% gillnet/50% trawl (dotted line). The species are: 1. Yellowtail snapper, 2. Atlantic croaker, 3. Common snook, 4. Atlantic sharpnose shark, 5. Atlantic silverside, 6. Atlantic croaker, 7. Atlantic croaker, 8. Atlantic croaker, 9. Atlantic croaker, 10. Atlantic croaker, 11. Atlantic croaker, 12. Atlantic croaker. The graphs show that the 100% gillnet method generally catches a higher percentage of the total catch for most species compared to the other two methods, especially for species like Atlantic croaker and Atlantic sharpnose shark.

<213> Escherichia coli

<400> 416

```

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taggtggtgt  taccggtggt  cagatccggg  aagatgaaca  cggtagcgcg  acctgcaacc     120
ggagagttcg  gcgctttgga  tttcgcaacg  tcagccatta  ccgcagcgtc  gtactgcagc     180
ggaccgtcga  tcatacggtc  a

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<210> 417

<211> 239

<212> DNA

<213> Escherichia coli

<400> 417

aattcagcag	ttgacagtgg	cataaacgta	actggtgact	tttgcccggc	atgacgcogg	60
gcttttttta	ttattccgtg	acttccagcg	tagtgaaggc	aaacttctcg	ccatcaaata	120
gcccctgact	ggtttagtttt	agcgcgggga	tactggcag	agaaagaaac	gccatctgaa	180
taaacggctc	atcgggtaac	ggaccgcatt	cacgggcggc	ggctttcaag	gcgtcaatt	239

<210> 418

 $\langle 211 \rangle$ 223

<212> DNA

<213> Escherichia coli

<400> 418

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ttttattatt	atggggaagg	tgttatttat	gagtttcatt	tatgccgtaa	cgacaatgaa	120
ctcggaatt	agtataagca	gcgcgagaat	aataatcatt	gtgcaaatgc	taatttaatt	180
aatactattt	aaatatattt	ttgagcatat	gcacataagg	ttg		223

<210> 419

<211> 223

<212> DNA

<213> Escherichia coli

<400> 419

tttttttttt	ogtcaacggt	gtccagaatc	attttattta	cctcgggtag	ttatgctgat	60
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ctcggaatt	agtataagca	gcgcgagaat	aataatcatt	gtgcaaatgc	taatttaatt	180
aatactattt	aaatatattt	ttgagcatat	gcacataaag	ttg		223

<210> 420

<211> 212

<212> DNA

<213> Escherichia coli

 $\langle 400 \rangle$ 420

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cctcgggtac	ttatgctgat	ttttattatt	atggggaagg	tgttatttat	gagtttcatt	120
tatgccgtaa	cgmcaatgaa	ctcgggaatt	agtataagca	gcgcgagaat	aataatcatt	180
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 $\langle 210 \rangle$ 421

<211> 438

<212> DNA

<213> Escherichia coli

<400> 421
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agcggggcgg agagctgttt cagttcggcg ggtaaccctt caatccattt gccgccagtc 180
cacagcaaca tgatgcctct gtacaaccct aacgtgccaa ggggtggcaac aatggcaggg 240
atcttttagcc acgogaccag gacaccgttg aaaaatcccg cgagcaaacc aagcagtaaa 300
gtcgcgacac aagcaacagg tagtgaatat cctgcgttca gtaacatccc caacagcacc 360
gcgcacattc cgggtaatcg aaccccactt gaaacatcaa tattgsgsgt aagcattwcc 420
aagcgttcgs gcccatkg 438

<210> 422
<211> 682
<212> DNA
<213> Escherichia coli

<400> 422
aattcccggg gatccgtcga ccgtgcgctt ccggttgtgg caaccgcgga aatggcgcg 60
cggtaagtat ggcggggtta ttcttcccc gttgaggaca ccgggttgtc aggttgacca 120
tacgtttaag tgacaacccc gctgcaacgc cctctgttat caattttctg gtgacgtttg 180
gcggtatcag ttttaactcg tgactgctct gccgcccttt ttaaagtga tttgtgatg 240
tggtgaatgc ggctgagcgc acgcggaaca gttaaaacca aaaacagtgt tatgggtgga 300
ttctctgtat ccggcggtta ttgttaactg gttaacgtca cctggaggca ccaggcactg 360
catcacaaaa ttcatgttg aggacgcgat aatgaaaacg ttattacca acgttaatac 420
gtctgaaggt tgttttgaaa ttggtgtcac tatcagtaac ccagtattta ctgaagatgc 480
cattaacaag agaaaacaag aacgggagct attaaataaa atatgcattg tttcaatgct 540
ggctcgttta cgtctgatgc caaaaggatg tgcacaatga attcagcatt tgtgcttgtt 600
ctgacagttt ttcttgtttc cggagagcca gttgatattg cagtcagtgt tcacaggaca 660
atgcaggagt gatgactgca gc 682

<210> 423
<211> 600
<212> DNA
<213> Escherichia coli

<400> 423
ggggatccga ttgtgactgc totgcccgc tttttaaagt gaattttgtg atgtggtgaa 60
tgcggtgag cgcaacgcga acagttaaaa caaaaaacag tggtatgggt ggattctctg 120
tatccggcgt taattgttaa ctgggttaacg tcacctggag gcaccaggca ctgcatcaca 180
aaattcattg ttgaggacgc gataatgaaa acgttattac caaacgttaa tacgtctgaa 240
ggttgttttg aaattggtgt cactatcagt aaccagtat ttactgaaga tgccattaac 300
aagagaaaaa aagaacggga gctattaaat aaaatatgca ttgtttcaat gctggctcgt 360
ttacgtctga tgccaaaagg atgtgcacaa tgaattcagc atttgtgctt gttctgacag 420
tttttcttgt ttccggagag ccagttgata ttgcagtcag tggtcacagg acaatgcagg 480
agtgtatgac tgcagcaacc gaacagaaaa ttcccgttaa ctgttaccg gtcgataaag 540
ttattcacca ggataatatc gaaatcccgg caggtcttta aacagttccg taataaataa 600

<210> 424
<211> 100
<212> DNA
<213> Escherichia coli

<400> 424
gggatccagc aagaagatgc ggttgtaccg tcatcacgca gatgcgcaaa gctactcagc 60
aactgacctt tottgcgaat aagcacgcca ttagcgtcat 100

<210> 425

<211> 465
<212> DNA
<213> Escherichia coli

<400> 425
tcgcgtgttt accttcaaca tcggtaactt tctggcggat agtttcacgg taagcaacct 60
gcggtttacc tacgttcgct tcaacgttga attcacgctt catacgggtca acgatgatgt 120
cgagggtgcag ttgcgccata ccgcgatga tgggtctgggt agattcttcg tcagtccata 180
cacggaaaaga cgggtcttct ttagccagac ggcccagagc cagacccatt tttcctgggt 240
cagctttgggt tttcgggttca actgcgatgg agattaccgg ctccagggaat tccatacgtt 300
ccagaatgat cggcgcaccc ggggtcacaca ggggtgtcacc agtgggttacg tctttcagac 360
cgatagcagc agcgatgtcg ccgcgcgcaa cttctttgat ctcttcacgt ttgttagcgt 420
gcatctgaac gatacgaccg aaacgctcac gtgcagcttt cacgg 465

<210> 426
<211> 653
<212> DNA
<213> Escherichia coli

<220>
<221> misc_feature
<222> (1)...(653)
<223> n = A,T,C or G

<400> 426
tgatcggctc aagcagaact ggtttcgctt tcttaaagcc ttctttaaag gcgatagaag 60
cagccagttt aaacgccagt tcagaggagt caacgctatg gtaagaaccg aagtgcagac 120
gaatacccat gtctactacc gggtagcctg ccagcggacc tgctttcagc tgttcctgga 180
tacctttatc aacggccggg atgtattcgc cagggattac accaccttta atgtcgttga 240
tgaactcgta gcctttcggg tttgaaccog gctccagcgg gtacatgtcg ataacaacat 300
gaccatactg accacgacca ccagactgtt tcgcgtgttt accttcaaca tcggtaactt 360
tctggcggat agtttcaagg taagcaacct gcgggtttacc tacgttcgct tcaacgttga 420
attcacgctt catacgggtc acgatgatgt cgagggtcag ttcgccatac ccgcgatgat 480
ggctgggtag attcttcgtc agtccataca cggnaagacg ggtcttnttt agccagacgg 540
gccagagnca gacccatttt tttctggcag ctttggnttc ggtcaactgc gatggaaata 600
cccggctcaa ggaattcata cgtttcanaa tgatcggggc attccgggtc aca 653

<210> 427
<211> 268
<212> DNA
<213> Escherichia coli

<400> 427
ctttcttaaa gccttcttta aaggcgatag aagcagccag tttaaacgcc agttcagagg 60
agtcaacgtc atggttaagaa ccgaagtgcg gacgaatacc catgtctact accgggtagc 120
ctgccagcgg acctgctttc agctgttcct ggataccttt atcaacggcc gggatgtatt 180
cgccagggat tacaccacct ttaatgtcgt tgatgaactc gtagcctttc gggtttgaac 240
ccggtccag cgggtacatg tcgataac 268

<210> 428
<211> 330
<212> DNA
<213> Escherichia coli

<400> 428
gttttgggga gatgtaaggg ctaatctgaa tggctgcatt ccttgtttaa ggaaaaacga 60
atgactgatt gccgatacct gattaaacgg gtcatacaaa tcatcattgc tgttttacag 120

ctgatccttc	tgttcttata	acacaaggaa	acgtacttaa	ggtgcgtccg	gtgaaccagt	180
cggacgcacc	tttaataact	ataaataagt	gtctgggcag	atactatata	aattaactta	240
gtgaatgatt	atgctaagt	catcaattaa	ataaatataa	tggcgттааg	gcttcccagt	300
aatataatta	atactctact	tccagagtag				330

<210> 429
 <211> 465
 <212> DNA
 <213> Escherichia coli

<400> 429						
gttttgggga	gatgtaagg	ctaacttgaa	tggctgcatt	ccttgtttaa	ggaaaaacga	60
atgactgatt	gccgatacct	gattaaacgg	gtcatcaaaa	tcattcattgc	tgttttacag	120
ctgatccttc	tgttcttata	acacaaggaa	acgtacttaa	ggtgcgtccg	gtgaaccagt	180
cggacgcacc	tttaataact	ataaataagt	gtctgggcag	atactatata	aattaactta	240
gtgaatgatt	atgctaagt	catcaattaa	ataaatataa	tggcgттааg	gcttcccagt	300
aatataatta	atactctact	tccagagtag	aatattaaat	tttatccgcg	tgggtgcatca	360
gcacaaatth	atcccacaac	tgttcttctg	tctcgacatg	cgcgggatct	ttcacaatag	420
tattggggat	cgggcacacc	ttctggcagg	ttgggtgtctc	gtagt		465

<210> 430
 <211> 379
 <212> DNA
 <213> Escherichia coli

<400> 430						
aatctgaatg	gctgcattcc	ttgtttaagg	aaaaacgaat	gactgattgc	cgatacctga	60
ttaaaccggg	catcaaaaatc	atcattgctg	ttttacagct	gacccctctg	ttcttataac	120
acaaggaaac	gtacttaagg	tgcgtccgg	gaaccagtcg	gacgcacctt	taataactat	180
aaataagtgt	ctgggcagat	actatataaa	ttaacttagt	gaatgattat	gctaattgtca	240
tcaattaaat	aaatataatg	gcgttaaggc	ttcccagtaa	tataattaat	actctacttc	300
cagagtagaa	tattaaatth	tatccgcgtg	gtgcattcagc	acaaatttat	cccacaactg	360
ttcttctgtc	tcgacatgc					379

<210> 431
 <211> 443
 <212> DNA
 <213> Escherichia coli

<400> 431						
aagatgatgt	gatgagaaag	tcaatttgaa	taagacaata	ttaagagcta	aaaaaatgtc	60
aaaaaacact	aaatcaaaaa	ataatggcat	tagaaaaat	aatgcgaaaa	cggaggtgaa	120
attagtttat	ttcaaatgag	gaaaatctcc	cggcgaaaaa	accgggagat	gaaagtgtga	180
tgggtatcaa	ataaacaca	gaggagaaat	ttttaacgca	gccattcagg	caaatcgth	240
aatcccattg	cctggcggat	aagttgcggc	ttaacgccag	gaagcgtgtc	ggccagtttc	300
aaaccaatat	cacgcagcag	ttttttcgcc	ggattggtag	cggaaaaacag	atcgcggaat	360
ccctgcatac	cagccagcat	caacgccgca	ctgtgcttgc	ggctacgctc	atagcgacgc	420
agataaatgt	actgcccgat	gtc				443

<210> 432
 <211> 638
 <212> DNA
 <213> Escherichia coli

<400> 432						
cagggggtth	gttgtgggca	atgatgcatt	taagttatcg	tctgcagata	gaggagatat	60
tacaataaac	aacgaatcag	ggcatttgat	agtcaatacc	gcaattctat	caggagatat	120

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agtcactcta agaggaggag aaattaggtt ggtattatag cttgtgcgcg ccatgattgg 180
cgcgcaatth aaacttagtg ctttacatcg ctattgtctt gatttctttg aattattttta 240
taaattaaaa aaacgactgt tatgtataag caaagggtccg aacgaaaaat acattccaaa 300
taaagtcttg cttaaatctc tatatccttc cccgaaaaat gacacataaa attgagatat 360
tccaaaaaga gatactacaa ataaagatgc ctttattttta ttatttctaa taaaaataga 420
agcaataaaa aataataaca atgatataaa tctaagtgtt ttaaatatat tgtctttttat 480
gttagtaata gtcgttagta tgtttgattc tccatatatt acgtgtagtt ttttatatac 540
atggaaataa ttttctttat actgagacat cacaccatca tcaaattggaa gtttgaagat 600
ggtgcttggt ttgctaacca ataaaaagag tgcattcg 638

```

<210> 433
 <211> 299
 <212> DNA
 <213> Escherichia coli

```

<400> 433
ctttacctgg catgatccac ttcgccagaa taccggcaat aagcccaaaa ataatccatg 60
acagaatgcc cattgtttcc tcacttatct gttttgcatt agcggggttag tcgctgataa 120
aaagcatagc acaacatcgg gagggcaaga tttgtgacga gcatcacgga gggttttttg 180
cgatggcgca gaaattgcgc catcaacgat cagtgataat taccaaccac aaacatcatg 240
ttcgttttcc gtgtcataag aacgtacggt attcaccaga tcttttatca cttcagccg 299

```

<210> 434
 <211> 388
 <212> DNA
 <213> Escherichia coli

```

<400> 434
gaaaaaggag gcaatatcgg gtaaaggcat tagcccgacg aatacgtcgg gctacaaata 60
ttattgtgct gcagggtgtt tagcgggttg ttgatccaca ggttctaact ggaagaccac 120
atcgacctga tcatcaaact gaatagcggc ctgctcgtaa gtttctctgg cggacaccgg 180
cgcgccatcg gctttcatca tccgcacatc tgggctgggc tgatagttag aaacatggta 240
gcgcacgcta tataccggcc ccagtttacg atgaaagcgg ttcgccagtt cctgcgcctg 300
atgaatcgcg ttatcaatcg ctgccttacg cgttttgtct ttataggcat ccggctgcgc 360
cacgccagc gacacagaac gaattccc 388

```

<210> 435
 <211> 351
 <212> DNA
 <213> Escherichia coli

```

<400> 435
ctatccttga tgaaaaccgc agcaaagata ggtgattacg tcatggtttt acagaaaatt 60
acagaaaaag gaggcaatat cgggtaaagg cattagcccg acgaatacgt cgggctacaa 120
atattattgt gctgcagggt ttttagcggg ttgttgatcc acaggttcta actggaagac 180
cacatcgacc tgatcatcaa actgaatagc ggctgctcg taagtttctt gggcggacac 240
cggcgcggca tcggctttca tcatccgcac cattgggctg ggctgatagt tggaacatg 300
gtagcgcacg ctatataccg gccccagttt acgatgaaag ccgttcgcca g 351

```

<210> 436
 <211> 762
 <212> DNA
 <213> Escherichia coli

<220>
 <221> misc_feature
 <222> (1)...(762)

<223> n = A,T,C or G

<400> 436

aattatgaaa	cactgtctgg	aatcgtctga	atgaaggga	catttgcgag	cacgcaccca	60
gtaataaacac	aggaaactat	tttatctacg	cgttagcgat	agactgcttg	catggcgaaa	120
ggaggtaacg	cgacgatttc	agcgggacgc	tgaacggga	aagcccctcc	cgaggaagg	180
gccataaata	aggaaaggg	catgatgaag	ctactcatca	tcgtgggtgct	cttagtcata	240
agcttccccg	cttactaaga	ctaccagggc	gggggaaacc	ccgctctacc	ctcactcctg	300
aaagtatgcc	ttcacgataa	gattgtcaat	ccgcaggctt	tgtagtctgc	gatcctgcc	360
gcaaataattc	tttgcgagtc	gttaacgaat	aatcacagag	gaaactatct	tattcacgcg	420
ttagcgatag	actgcattca	gggagaaagg	aggtaagccg	atgatttcag	cgggacgctg	480
aaacgggaaa	gcctctcccc	gagaagagg	cttttaataa	ggaaaggggt	atgatgaagc	540
acgtcatcat	actggtgata	ctcttagtga	ttagcttcca	ggcttactaa	gaacaccagg	600
gggaggggga	aacctcttcc	taacctcac	ttctgaaatt	gggtgctatg	acgctggcgt	660
tactgcttan	cgctaccagt	ttgtctgcc	tggcggttgt	aacgccagat	cggtaccctg	720
ttggatattt	taatgaaagc	cgacaaatca	atcancgtga	cg		762

<210> 437

<211> 292

<212> DNA

<213> Escherichia coli

<400> 437

cacatttgcg	agcacgcac	cagtaataac	acaggaaact	attttatcta	cgcgttagcg	60
atagactgct	tgcattggcg	aaggaggtaa	gccgacgatt	tcagcgggac	gctgaaacgg	120
gaaagcccct	cccaggaag	gggccataaa	taaggaaagg	gtcatgatga	agctactcat	180
catcggtgtg	ctcttagtca	taagcttccc	cgcttactaa	gactaccagg	gcgggggaaa	240
ccccgctcta	ccctcactcc	tgaagtatg	cttcacgat	aagattgtca	at	292

<210> 438

<211> 631

<212> DNA

<213> Escherichia coli

<400> 438

atttacactt	tttacgaaat	catgggatca	ctaacaaaat	atcgcttgct	agttatattg	60
tatggcagga	aagatatgcg	actgatatta	cagatcccca	aagtggagag	tttatgacca	120
ttaaaaataa	gatgttgctg	ggtgcgcttt	tgtgtgttac	cagtgcgcgc	tgggccgcac	180
cagccaccgc	gggttcgacc	aatacctcgg	gaatttctaa	gtatgagtta	agtagtttca	240
ttgtcgactt	taagcatttc	aaaccagggg	acaccgtacc	agaaatgtac	cgtaccgatg	300
agtacaacat	taagcagtgg	cagttgcgta	acctgcccgc	gcctgatgcc	gggacgcact	360
ggacctatat	gggtggcgcg	tacgtgttga	tcagcgacac	cgacggtaaa	atcattaaag	420
octacgacgg	tgagattttt	tatcatcgct	aaaaaaagcc	ccctcatcat	gagggggaaa	480
tgcagacacc	ttgttatattt	ttattattag	ccacttgctc	gtcttgcttg	ttattagtcg	540
tatttcacgt	tgattaatgc	ggttgcctcc	agtgcgccag	atttaacttt	gtttgtatcg	600
tagacgtagt	aactggctgt	tatcggaatt	g			631

<210> 439

<211> 566

<212> DNA

<213> Escherichia coli

<400> 439

tatggcagga	aagatatgcg	actgatatta	cagatcccca	aagtggagag	tttatgacca	60
ttaaaaataa	gatgttgctg	ggtgcgcttt	tgtgtgttac	cagtgcgcgc	tgggccgcac	120
cagccaccgc	gggttcgacc	aatacctcgg	gaatttctaa	gtatgagtta	agtagtttca	180
ttgtcgactt	taagcatttc	aaaccagggg	acaccgtacc	agaaatgtac	cgtaccgatg	240

```

agtacaacat taagcagtgg cagttgcgta acctgccgcg gcctgatgcc gggacgcact 300
ggacctatat ggggtggcgcg tacgtgttga tcagcgacac cgacggtaaa atcattaaag 360
cctacgacgg tgagattttt tatcatcgct aaaaaaagcc ccctcatcat gagggggaaa 420
tgcagacacc ttgttatttt ttattattag ccacttgctc gtcttgcttg ttattagtcg 480
tatttcacgt tgattaatgc ggttgccctcc agtgcgccag atttaacttt gtttgtatcg 540
tagacgtagt aactggctgt atcgaa 566

```

<210> 440
 <211> 339
 <212> DNA
 <213> Escherichia coli

```

<400> 440
cgtattcaca tccttttgat tgggtgataac atgcgaatcg gtattatttt tccggttgta 60
atcttcatta cagcggtcgt attttttagca tgggttttta ttggcggcta tgctgccccg 120
ggagcataaa gatgaaaaaa acaacgatta ttatgatggg tgtggcgatt attgtcgtac 180
tcggcactga gctgggatgg tggtaacgtc acctctaaaa aatagcaaag gctgcctgtg 240
tgacgccttt gtgcaattta agcgtttaact tttaatcttc ctgtagataa atagcacgac 300
aatcgcacca ataacggcaa ccacgaagct gccaaaatt 339

```

<210> 441
 <211> 376
 <212> DNA
 <213> Escherichia coli

```

<400> 441
catgaatatt taaaaaggaa aacgacatga aaccgaagca cagaatcaac attctccaat 60
cataaaatat ttccgtggag cattttatta ttgaatatag aggtttaact ccggtaaaaa 120
acaaagaagc attgaatgca gggaaaaata atatggccat aaaaaacatc gaaagaaact 180
cttttaattt aacatgtaaa cgcattggtt atctcatat cacgggtgga gtgttaagaa 240
catacataaa tggagtcatt ttttcccttt tccatttatt aagttcctgt tgccgtttta 300
gtccatctct aattgcattt ttttaatttt ctgataaatg gcatttagca tcgatttcat 360
ttaaacaac tgtaca 376

```

<210> 442
 <211> 446
 <212> DNA
 <213> Escherichia coli

```

<400> 442
ttacgatagc tattagtaaa aatataagag ttagctgtat tgttatgtct gtggcgaaat 60
tgactacott cgtttttttg attaagaatg attttattat cgtaagtaaa attacatgaa 120
tatttaaaaa ggaaaacgac atgaaaccga agcacagaat caacattctc caatcataaa 180
atatttccgt ggagcatttt attattgaat atagaggttt aactccggtg aaaaacaaag 240
aagcattgaa tgcagggaaa aataatatgg ccataaaaaa catcgaaaga aactctttta 300
atttaacatg taaacgcatg gttaatcctc atatcacggg tggagtgtta agaacataca 360
taaattggagt catgttttcc cttttccatt tatcaagttc ctggttgccgt tttagtccat 420
ctctaattgc atatttttaatt ttttct 446

```

<210> 443
 <211> 388
 <212> DNA
 <213> Escherichia coli

<220>
 <221> misc_feature
 <222> (1)...(388)

<223> n = A,T,C or G

<400> 443

tcaccccggt	gccgattttc	aggcatcctg	atttaactta	gcacccgcaa	cttaactaca	60
ggaaaacaaa	gagataaatg	tctaatacctg	atgcaaatcg	agccgatttt	ttaatcttta	120
cggactttta	cccgcctggt	ttattaattg	caactgtnatc	cgggcgcttcg	cccgccttta	180
tcacaatagg	ctgtgtagcc	tgggcctggt	tctctttcac	ccgcgccaga	gcggcagcaa	240
tcgcatcttt	atctttggct	gcagggttga	cggtcgcgct	cttatgtcgt	tcaaggcgag	300
ccgctttttc	gcgctccaga	cgagcctggc	gcgcttcgaa	acgcgctttg	gcttctgcgg	360
cncgcttttc	ttcctgacga	atagccgc				388

<210> 444

<211> 209

<212> DNA

<213> Escherichia coli

<400> 444

aattttaata	acgctatctg	cggataaagc	agaatagggtg	gttaacccca	gacataaacc	60
gaggaaaata	atgttattgt	atttcataat	ctattgttcc	ttagcgacag	attgctgtct	120
gctggttcag	taaggtagca	ggagaaactt	caggaagctt	gtactcgaca	atacagtttg	180
agtttttatc	tttgcccat	gaaacctgt				209

<210> 445

<211> 341

<212> DNA

<213> Escherichia coli

<400> 445

catcctcaat	accgttaaat	gcaacccgaa	ccccggttgt	ccctttgctg	cattcaactta	60
acgtaatctg	aaaagggacg	gctggacttg	tgctaccggt	cgttggaaat	tgtctggcac	120
tgtttttttg	gagatctacg	gtaaaattaa	gcgaatccga	tgagactgtg	cagccataat	180
cgaggacgcg	cccgtcaatt	ttaataacgc	tatctgcgga	taaagcagaa	taggtgggta	240
acccagaca	taaaccgagg	aaaataatgt	tattgtattt	cataatctat	tgttccttag	300
cgacagattg	ctgtctgctg	gttcagtaag	gtaccaggag	a		341

<210> 446

<211> 697

<212> DNA

<213> Escherichia coli

<400> 446

agatttactg	ccaatttccg	gcagatcgga	aaggggttaam	ccatattgat	ccataagggt	60
acgaatcmcg	ggctataccg	ccaggcatgg	cttgagccat	ggcattaaat	tccgcaaatt	120
cgggcgctga	ttcttccac	gcgggtattt	tggcacacac	cagatccagc	aaggggtttt	180
caggatcggt	gagcagcaga	tgatctacca	gttccagcgc	ctgggtgtat	tgttcctcgt	240
tctgaatacc	cgccagaaaa	ggtgccacag	cagttagctt	ttctcctgct	tgcaagatgt	300
cggcaatcgc	aatcattttt	tccccttagt	acgatgaaca	gcggtaaaga	aatcgtattc	360
tttatgogtc	ataacttcac	gtatgtagca	cttttgcgat	tcaaaaaaga	ccattgctac	420
aacacgtaat	tcattgcccc	caacattgaa	aacataatgc	ttatccagat	atttgaagtt	480
atccagagat	gggaatactg	cttttaatga	ctcaggtttt	ttgaaatata	ccttagcaat	540
cgtgktcccc	agagccacca	actccgtttt	atggtgcggg	tatttttccg	cagcatcttt	600
caatgctttt	tgagttatca	ggtgcattct	tcatcacgct	cgtkgmcaaa	ttggcaatat	660
gataacatcc	gttgccagat	tggcacggat	gaattat			697

<210> 447

<211> 215

<212> DNA

<213> Escherichia coli

<400> 447

```
aattaataac ttttcgtag gcagttttgg gtgtgagttg caagagggga gactactgaa    60
taactcaagt tttataatcg aggggaaaat ggtgatggcg ttcatagcaa aacgccctca    120
accataaagg tcgagggcgc ttaagatgtt aaaaacccgc tatccgttaa aaaacaatgt    180
tcaactaagg tcagtacat tgcgctaaaa aagcg                                215
```

<210> 448

<211> 395

<212> DNA

<213> Escherichia coli

<400> 448

```
gcattattca tgagaaatgt gtatcgtaaa tcaactgaaa ttaacgcaac catttggtat    60
ttaaggttta attatctgtg tgtgatattt tattgaatgt tttaaatatt gtttttattg    120
gcattgctat aatattgggt atcatttgct gaatggattc agtcttaatg agtgggtttt    180
taagggacag gcatagagta atgatacgta tgcataacca acatctttac tcattatgtc    240
attgaatgtt gacgctatgt gtttatgagg gagaggattt ttcagttgat ctggattgtt    300
aaattcatat aatgcgcctt tgctcatgaa tggatgccag tatgtagtgg gaaattataa    360
atattgaaat agtccaacta cttctttatt accaa                                395
```

<210> 449

<211> 641

<212> DNA

<213> Escherichia coli

<220>

<221> misc_feature

<222> (1)...(641)

<223> n = A,T,C or G

<400> 449

```
ataatcaggt aagaaaaggt gcgcggagat taccgtgtgt tgcgatatat tttttagttt    60
cgcgtagcaa tacatcagtg gcaataaaac gacatatcca gaaaaatata cactaagtga    120
atgatattct ccgatttatt ttaatcgttt atggataacg gcaaagggct tcgttttttc    180
ctatacttat tcagcaactca caaataaagg aacgccaatg aaaattatac tctgggctgt    240
attgattatt ttcttgattg ggctactggg ggtgactggc gtatttaaga tgatatttta    300
aaattaatta atgtcatcag gtccgaaaat aacgagaata tttcagtctc tcacctgttt    360
gcgctcctgt catgtgcatt gcttcatata atcactggcg caaggagcgc cgcaggcgna    420
gnntgcncgn cgncccaact naccatgc cgaacttcag aantgaaaac nccntaacnc    480
cgatngtcgg cggngcctc cccatgcnan agtangggaa ntgccangcg ncnntataaa    540
cgaaaggctn attncaaaga ctgggccttn cntttatctg atgtttgtcg gagaacgctc    600
tcctgagnan gacaaatncc gccgggagcg gatttgaacn t                                641
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<210> 450

<211> 314

<212> DNA

<213> Escherichia coli

<220>

<221> misc_feature

<222> (1)...(314)

<223> n = A,T,C or G

<400> 450

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gaactacgag taagaatagc tncgaattcc cgtttatgga taacggcaaa gggcttcggt    60
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ttttcctata	cttatttcage	actcacaaat	aaaggaacgc	caatgaaaat	tatactctgg	120
gctgtattga	ttattttccct	gattggggcta	ctgggtgggta	ctggcgtatt	taagatgata	180
ttttaaaatt	aattaatgtc	atcagggtccg	aaaataacga	gaatatttca	gtctctcatc	240
ctgttgcgct	cctgtcatgt	gcattgcttc	atataatcac	tggcgcaagg	agcgcgcagg	300
gggntntnnt	cttt					314

<210> 451
 <211> 236
 <212> DNA
 <213> Escherichia coli

<400> 451						
atatacacta	agtgaatgat	atcttccgat	ttatcttaat	cgtttatgga	taacggcaaaa	60
gggcttcggt	ttttcctata	cttatttcage	actcacaaat	aaaggaacgc	caatgaaaat	120
tatactctgg	gctgtattga	ttattttccct	gattggggcta	ctgggtgggta	ctggcgtatt	180
taagatgata	ttttaaaatt	aattaatgtc	atcagggtccg	aaaataacga	gaatat	236

<210> 452
 <211> 418
 <212> DNA
 <213> Escherichia coli

<400> 452						
cggagattac	cgtgtgttgc	gatataat	ttagtttcgc	gtggcaatac	atcagtggca	60
ataaaacgac	atatccagaa	aaatatacac	taagtgaatg	atatcttccg	atttatctta	120
atcgtttatg	gataacggca	aagggtctcg	tttttcccta	tacttattca	gcactcacia	180
ataaaggaac	gccaatgaaa	attatactct	gggctgtatt	gattattttc	ctgattgggc	240
tactggtggt	gactggcgta	tttaagatga	tattttaaaa	ttaattaatg	tcatcaggtc	300
cgaaaataac	gagaatat	cagtctctca	tcctgttgcg	ctcctgtcat	gtgcattgct	360
tcatataatc	actggcgcaa	ggagcgcgca	ggggcgcgcc	aatcgccgcc	gccccctg	418

<210> 453
 <211> 551
 <212> DNA
 <213> Escherichia coli

<400> 453						
aacaatttgc	ccatgcgctc	ggtcattgct	tgcattcgcc	ggccattttg	sgcgtccccg	60
cgaccgccat	tcgaactgta	atgggcgaat	cttcagttat	ggatttaggt	ggacaacgcg	120
cgctgcctaa	acggctggaa	gaagcgggtt	ttgcgtttcg	ctggtacgat	ttagaagagg	180
cgctggcgga	tgctgttcgc	tgatgtggtt	tacagcaaac	atccgccagt	taactccccg	240
tgttacagga	ttagtggctt	tgccgcgata	gatcgtctgg	tgaaagtcgg	gtcaccatca	300
taactaaactc	tcgtgtctaaa	cctctatcca	gcattctcctg	agcaatacgc	agggtctctt	360
cgtgttttgc	ctgcattgcg	ccttcttcac	gtaattctgtc	agcaatgggc	atcaagtttc	420
tccttttctt	gtgggtgcgcg	ttccgctatc	tcaccaataa	atgcacgaaa	acgctgggca	480
tcccctgttt	gtaatacgtg	attaaacagg	gcttttagct	gtctgtcatt	agtgtkccct	540
gtaactagca	g					551

<210> 454
 <211> 93
 <212> DNA
 <213> Escherichia coli

<400> 454						
tggtatctcg	gtgttgccga	tcttcatgat	atccagcccg	ccggaaactt	cttcccaaac	60
ggttttgcgt	ttatccattg	agtcacggaa	ctg			93

<210> 455
 <211> 232
 <212> DNA
 <213> Escherichia coli

<400> 455
 cgtgccgaga tgatcctgta accatcatca gttgtgaagt agtgattcac gacttcaagg 60
 cgcttttcaa aagggtatatt tggctttgac atattagggg ctattccatt tcatcgtcca 120
 acaaaatggg tgcagtacat actcgtttga aatcaacaca ggaggctggg aatgccgcag 180
 aaatatagat tacttttctt aatagtgtatt tgtttcacgc ttttattttt ca 232

<210> 456
 <211> 713
 <212> DNA
 <213> Escherichia coli

<220>
 <221> misc_feature
 <222> (1)...(713)
 <223> n = A,T,C or G

<400> 456
 ttagnnggatn naangccac ancctcgang gatctaggag gtagaatagc ttogaattcc 60
 ccagcagagc gcggccttct tcgtcagatt tcgcagtagt ggtaatggta atatccaaac 120
 cacgaacgcg gtcgacttta tcgtagtcga tttctgggaa gatgatctgc tcacggacac 180
 ccatgctgta gttaccacga ccgtcgaaag acttagcgga caggccacgg aagtcacgga 240
 tacgaggtac agcaatagt atcaggcgct caaagaactc ccacatgctg tcgccacgca 300
 gagttacttt acagccgacg ggatagccct gacggatttt gaagcctgca acagatttgc 360
 gtgcttttgt gatcagcggt ttttgaccgg agattgctgc caggctctgct gctgcgttat 420
 ccagcagttt tttgtcagcg atcgcttcac caacacccat gttcagggtg atcttctcga 480
 cccgagggac ttgcatgaca gaattgtagt taaactcagt catgagtttt ttaactactt 540
 cgtctttgta gtaatcatgc agtttcgcca tcgtactact ccatgtcggg gaacgctctc 600
 ctgagtagga caaatccgcc ggagccggat ttaacgttgc gaacaaccgn cccggagggg 660
 tggnggcagg accccgccat aactggcagc attaaattaa gcagaaggcc atc 713

<210> 457
 <211> 292
 <212> DNA
 <213> Escherichia coli

<400> 457
 tgaacagcag agatacggcc agtgcggcca atgttttttg tcctttaaac ataacagagt 60
 cctttaagga tatagaatag gggatatagc acgccagaat atcgtatttg attattgcta 120
 gtttttagtt ttgcttaaaa atattgttag ttttattaaa tgcaaaacta aattattggt 180
 atcatgaatt tggtgtatga tgaataaaat ataggggggt atagatagac gtcattttca 240
 tagggttata aatgcgacta ccatgaagtt ttttaattgaa agtattgggt tg 292

<210> 458
 <211> 282
 <212> DNA
 <213> Escherichia coli

<400> 458
 ttattaaatg caaaactaaa ttattggtat catgaatttg ttgtatgatg aataaaatat 60
 aggggggtat agatagacgt ctttttcata ggggtataaa tgcgactacc atgaagtttt 120
 taattgaaag tattgggttg ctgataattt gagctgttct attcttttta aatatctata 180
 taggtctgtt aatggatttt atttttacaa ttttttgtgt ttaggcataa aaaaatcaac 240

ccgccatatg aacggcggggt taaaatattt acaacttagc aa

282

<210> 459

<211> 300

<212> DNA

<213> Escherichia coli

<400> 459

tctgcgttcc	gctaaaaggt	gcaaagtctc	aggacgttgc	agcgttttgc	gtgaccgctc	60
ggggaaggca	aaattgcctc	tgggaaagca	ttgcgcgggg	tccggcgctc	atcaacaatc	120
ggggggcagc	aaggggctga	aacgggaaaag	cccctcccga	agaagggggc	ttgtataagg	180
aaagggttat	gatgaagctc	gtcatcatac	tggttgtgtt	gttactgtta	agtttcccga	240
cttactaaca	actcatcaga	ggggggagaa	atcctccctt	acccttgttc	ctttactcta	300

<210> 460

<211> 293

<212> DNA

<213> Escherichia coli

<400> 460

cggggtccgg	cgctcatcaa	caatcggggg	gcagcaaggg	gctgaaacgg	gaaagcccct	60
cccgaagaag	gggccttgta	taaggaaagg	gttatgatga	agctcgtcat	catactgggt	120
gtgttgttac	tggttaagttt	cccgacttac	taacaactca	tcagaggggg	gagaaatcct	180
cccttaccct	tgttcccttta	ctctaggttg	aaaaaacaac	agcgtcaata	ggcctgccat	240
gtacgaagcg	agatctgtga	accgctttcc	ggttagcctt	ttttatcctg	ttg	293

<210> 461

<211> 359

<212> DNA

<213> Escherichia coli

<400> 461

caacacagga	ggctgggaat	gccgcagaaa	tatagattac	tttctttaat	agtgatttgt	60
ttcacgcttt	tattttttcac	ctggatgata	agagattcac	tgtgtgaatt	gcatattaaa	120
caggagagtt	atgagctggc	ggcgttttta	gcctgcaaat	tgaaagagta	agagtcttcg	180
gcgggaaatt	attccgcctt	tacttacggc	gttgcgcat	ctcattgcac	ccaaatttat	240
tcttcacaaa	aataataata	gattttatta	cgcgatcgat	tattttattc	ctgaaaacaa	300
ataaaaaaat	ccccgccaaa	tggcagggat	cttagattct	gtgcttttaa	gcagagatt	359

<210> 462

<211> 673

<212> DNA

<213> Escherichia coli

<400> 462

gcaacccatg	tcttgacctg	ggttcggggg	acacccaaaac	gtgccgagat	gatcctgtaa	60
ccatcatcag	ttgtgaagta	gtgattcacg	acttcaaggc	gcttttcaaa	agggtatattt	120
ggctttgaca	tattaggggc	tattccattt	catcgtccaa	caaaatgggt	gcagtacata	180
ctogttggaa	atcaacacag	gaggctggga	atgccgcaga	aatatagatt	actttcttta	240
atagtgattt	gtttcacgct	tttatttttc	acctggatga	taagagattc	actgtgtgaa	300
ttgcataatta	aacaggagag	ttatgagctg	gcggcgtttt	tagcctgcaa	attgaaagag	360
taagagtctt	cggcgggaaa	ttattccgcg	cttacttacg	gcgttgcgca	ttctcattgc	420
acccaaattt	attcttcaca	aaaataataa	tagattttat	tacgcgatcg	attattttatt	480
tcttgaaaac	aaataaaaaa	atccccgcca	aatggcaggg	atcttagatt	ctgtgctttt	540
aagcagagaa	tacaggctgg	ttacgttacc	agctgccggg	ccttttagcg	cgctttcgat	600
ggtgaaggac	actttctgac	cttcgtccag	agattttgtaa	ccatcgttct	ggatagcaga	660
gaagtgtacg	aac					673

<210> 463
 <211> 630
 <212> DNA
 <213> Escherichia coli

<400> 463
 tgggtggcatt ggttgctgga gagagaaaac ccccgcacgt tgcaggtatg cacctgacaa 60
 caccacgggg gctaattcttg actctagacc actcaagaat agccgcgaaa cgttgtcatt 120
 acaacacagg cggctatatg acgttcgcag agctgggcat ggccttcttg catgatttag 180
 cggctccggg cattgctggc attcttgcca gtatgatcgt gaactggctg aacaagcgga 240
 agtaacgtgt catgcggggc tcaggctgcc gtaatggcaa tttgcgcccg gaccaggccg 300
 caggggggaa actctgcggc ctttttcggt cttactgcgg gtaaggcacc cagtcgccgc 360
 cgttcaggcg aacgtacggg ttatcctggg attgaataac tactgcattt gagttctcgg 420
 agaccgggtg tgtttgtggc aacccactgg tgagtttttt ccagtcaaca ttgtcttcgg 480
 tgaaaatctt gccatcgaga acgcgaacca ccagatcgga gatagccagg aagctgctcg 540
 gttgttcgat gacaatcggg gccccctgat gcgggtgcctt catgccgaag aatttcaccc 600
 caacggggac gtcgggtgata gacgggctag 630

<210> 464
 <211> 391
 <212> DNA
 <213> Escherichia coli

<400> 464
 cttaggctgc tgattgtttt tttgtgcaat ggcgcggtat tagcgtcgtt gctgtcgatg 60
 gagagaatca taaacgtggg gaatgatgat tgtagcaag gaaaactgtc aaaaatcttc 120
 aaaaaatttg agggataagg ccggaatggc tccggccaga gggaagttaa ccgcgaagct 180
 gttgctgctt gagggctcgtt ttaaccagac gccaggcgct ccatacgcca aaaccgcgtc 240
 tggcccagcg gaccagcata ttaggatggc gaatcgtcca gatcgccatc acgctactgc 300
 caaccagcgc ccaggagcgc agacttagca gcatattcca gcgacgatcg taagcgctcg 360
 ttgtctccag ccattcacga cgactggcgg a 391

<210> 465
 <211> 625
 <212> DNA
 <213> Escherichia coli

<400> 465
 aacacaccac accataaacg gagggcaaata atgctgggta atatgaatgt tttaatggcc 60
 gtactgggaa taattttatt ttctggtttt ctggccgcgt atttcagcca caaatgggat 120
 gactaatgaa cggagataat cctcaccta accggcccct tgttacagtt gtgtacaagg 180
 ggcttgattt ttatgacggc gaaaaaaaaac cgccagtaaa ccggcggtga atgcttgcatt 240
 ggatagattt gtgttttgcg ttacgctaa caggcatttt cctgcactga taacgaatcg 300
 ttgacacagt agcatcagtt ttctcaatga atgttaaacg gagcttaaac tcggttaatc 360
 acattttgtt cgtcaataaa catgcagcga tttcttcggg tttgcttacc ctcatacatt 420
 gcccggtccg ctcttccaat gaccacatcc agaggctctt caggaaatgc gcgactcaca 480
 cctgctgtca cggtaatgtt gatatgcctt tcagaatgtg tgatggcatg gttatcgact 540
 aactggcaaa ttctgacacc tgcacgacat gcttcttcat cattagccgc tttgacaata 600
 atgataaatt cttcgccccg gtagc 625

<210> 466
 <211> 623
 <212> DNA
 <213> Escherichia coli

<400> 466

agatgattgc cggaacttg ttagcggcac gcaggcgcg gctcgcaccc ttaccctgct 60
 ctttacgtac ttctgcgttg atagtaaaca tttctttc 98

<210> 471
 <211> 259
 <212> DNA
 <213> Escherichia coli

<400> 471
 agcgcgaacg aagtogatgt gctgcagctt cggtttgtac gggtgacgct gtacgtcctg 60
 agctttaact ttgatttctt taccgtcaac aacgatggtc agaacttcgc tgtagaattc 120
 agcttttagct tgcattgtca tgactttgtc gtgatccagc tcgatagcca gcggcgcttc 180
 tttgccaccg tagatgattg ccggaactt gttagcggca cgcaggcggc ggctcgcacc 240
 cttaccctgc tctttacgt 259

<210> 472
 <211> 94
 <212> DNA
 <213> Escherichia coli

<400> 472
 aaaaacggcg taaagaaagg atgcaaacat gttaataaaa actcaaattg atcccacgta 60
 tatattacgc cgcaaaatcc ttacaataaa cagg 94

<210> 473
 <211> 174
 <212> DNA
 <213> Escherichia coli

<400> 473
 ttaattatta aaatagtgtg acgcgattat gtggttatgg gggtaaacad taaataaacc 60
 agcggggagg ggaggtaaag tgaaaaaata aaaagcggat aatcttaata agcaggccgg 120
 acagcatcgc catccggcac tgatacgagg tttatttcag ctcacacacc atcg 174

<210> 474
 <211> 138
 <212> DNA
 <213> Escherichia coli

<400> 474
 ctgtaaaaac gtcaaaaaga gtgttttatt aacagaagaa tggaggctctg acagatagta 60
 gtaatgcaaa aaaatggaga cttaagtga atgaacggga gtaaagcgaa aagactatag 120
 agtgaaggag aaattccc 138

<210> 475
 <211> 191
 <212> DNA
 <213> Escherichia coli

<400> 475
 tttgttggtg taatattcta ttgttatctt tatttataga tgtttatatt gcatgaggtg 60
 gtttttgagg agaagaatga ggaagatgcg tcgagccaca gaaacgtag ctttacatat 120
 agcggagggtg atgtgaaatt aatttacaat agaaataatt tacatatcaa acagttagat 180
 gctttttgtc g 191

<210> 476
 <211> 245

<212> DNA

<213> Escherichia coli

<400> 476

cggccattta	tacaggaaaa	gcctatgtca	gaacgtaaaa	actcaaaatc	acgccgtaat	60
tatctcgta	aatgttcctg	cccaaactgc	acccaagagt	cagaacacag	tttttcaaga	120
gtacaaaaag	gtgccctttt	gatctgccct	cattgcaaca	aagtattcca	gacaaatctt	180
aaagctgtag	cctgattgat	tttattagta	acaagtattt	tttatatttt	aataatatat	240
ttaa						245

<210> 477

<211> 319

<212> DNA

<213> Escherichia coli

<400> 477

aaattttcag	gtaccttgtc	accatacttt	tttttctgag	cattaatgat	attttgagct	60
tcttgaggat	ctttaactcc	ccacatttgg	tggaaagtat	tcatattaaa	aggaagggtg	120
aataatttgt	ctttataaat	cgccagtggg	gaattagtaa	aacgattaaa	ttctactaaa	180
tcattaacgt	aatcccatat	atatttatca	ttggtatgaa	aaatatgtgc	accatattta	240
tgaatctgga	taccctcaca	gtcctctgtg	taogcatttc	caccgatatg	atttcttttc	300
tcaatcacta	aaacttttt					319

<210> 478

<211> 149

<212> DNA

<213> Escherichia coli

<400> 478

gcagtgatcg	aagcgatgac	gaagtgtatg	gaaaaatcag	aaaaactcag	caaatcctga	60
tgactttcgc	cggacgtcag	gccgccactt	cgggtgcggtt	acgtccggct	ttctttgctt	120
tgtaaagcgc	caaatctgcc	gatttcaac				149

<210> 479

<211> 330

<212> DNA

<213> Escherichia coli

<400> 479

gaaagtatct	tcgttattga	catcactgga	aaatataact	tgcttttcat	tattaaactc	60
gaagcgcgta	ccgtatctgg	acaaacattt	atcgagctta	ccaaattcct	gaagagggtt	120
aactacagat	aacatttgcg	cgtcctttgc	agtaatgcc	gtcaaactcct	tgacgggcat	180
tatttagatt	aaattaccag	tatttcttcg	gagtgaagaa	tattaccagg	tatatttaac	240
acccacgttc	gcggaccagt	cttgatctac	gtcaccacca	ccgaggtagt	tagcatcggt	300
ataggcgctg	aagttcttgg	tgaagctaaa				330

<210> 480

<211> 191

<212> DNA

<213> Escherichia coli

<400> 480

tttttttcca	gcaacggagc	aaaagggttg	cccttggtgca	gctcagggtt	aaccacttta	60
actacgtggc	gaagaccggg	agatgtcggt	ttacatttaa	caactgccat	tgtattactc	120
ctccgactta	ctcagcgccg	ccaacgaagt	ccagattctg	gccttctttc	agggtgacgt	180
aagctttttt	c					191

0044370.012300

<210> 481
<211> 188
<212> DNA
<213> Escherichia coli

<400> 481
tccctttaac taccaggggtg ttaacgactt cgacttcgac ttcaaacagt ttctgcacag 60
cagctttgat ttctgctttg gtgcggtctt tagcaacttt gactacgatg gtgttggtt 120
tttccatcgc agtagacgct ttttcagaaa cgtgcggtgc acgcagcacc ttcagcagac 180
gttcttca 188

<210> 482
<211> 172
<212> DNA
<213> Escherichia coli

<400> 482
caaaggcgaa caaagcctgt gaagcccgaa ggctccacag acagtgctac ttgaaggcct 60
tactgtttct tcttaggagc gagcaccatg atcatctggc ggccttcgat cttcgttggg 120
aaggattcga ccaactgccag ttcttgcaaa tcgtctttca cgcgattaag ca 172

<210> 483
<211> 266
<212> DNA
<213> Escherichia coli

<400> 483
tgagaaaaac gggtagattga taaagcaatc atcgttctag gggcgttaat tgcgctgctg 60
gaactgatcc gctttctgct tcagcttctg aactgatagc ggaaacgtaa ttaagggcta 120
agagcacact actcttagcc ctttaacatt taacgcattg tcacgaactc ttctgccgcc 180
gttggggtgaa tggcgacggt attgtcgaag tcttttttgg ttgcccccat cttcagcgcc 240
accgcgaagc cctgcaacat ttcgtc 266

<210> 484
<211> 259
<212> DNA
<213> Escherichia coli

<400> 484
cgcaggcagc tgatgggtcaa caggatgaga gaaaccacaga gacagggttaa tcacattgcc 60
tttaaccgct gcacggtaac ctacaccaac cagctgcagc ttcttagtga agccttcggt 120
aacaccgata accattgagt tcagcagggc acgcgcggta ccagcctgtg cccaaccgtc 180
tgcgtaacca tcacgcggac cgaaggtcag ggtattatct gcatgtttaa cttcaacagc 240
atcgttgaga gtacgagtc 259

<210> 485
<211> 73
<212> DNA
<213> Escherichia coli

<400> 485
caggtcggaa cttaccgcag aaggaatttc gctaccttag gaccgttata gttacggccg 60
ccgtttaccg ggg 73